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SUBSTITUTE CHEMICAL PROGRAM

INITIAL SCIENTIFIC AND MINIECONOMIC REVIEW OF CAPTAN

MIDWEST RESEARCH INSTITUTE

PREPARED FOR
ENVIRONMENTAL PROTECTION AGENCY

APRIL 1975

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  static water
city filtered water
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APRIL 1975

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS
CRITERIA AND EVALUATION DIVISION
WASHINGTON, D.C. 20460

EPA-540/1-75-012

This report has been compiled by the Criteria and Evaluation Division, Office of Pesticide Programs, EPA, in conjunction with other sources listed in the Preface. Its contents do not necessarily reflect the views and policies of the Environmental Protection Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

PREFACE

The Alternative (Substitute) Chemicals Program was initiated under Public Law 93-135 of October 24, 1973, to "provide research and testing of substitute chemicals." The legislative intent is to prevent using substitutes, which in essence may be more deleterious to man and his environment, than a problem pesticide (one that has been suspended, cancelled, deregistered or in an "internal review" for suspected "unreasonable, adverse effects to man or his environment"). The major objective of the program is to determine the suitability of substitute chemicals which now or in the future may act as replacements for those uses (major and minor) of pesticides that have been cancelled, suspended, or are in litigation or under internal review for potential unreasonable adverse effects on man and his environment.

The substitute chemical is reviewed for suitability considering all applicable scientific factors such as: chemistry, toxicology, pharmacology and environmental fate and movement; and socio-economic factors such as: use patterns and cost and benefits. EPA recognizes the fact that even though a compound is registered it still may not be a practical substitute for a particular use or uses of a problem pesticide. The utilitarian value of the "substitute" must be evaluated by reviewing its biological and economic data. The reviews of substitute chemicals are carried out in two phases. Phase I conducts these reviews based on data readily accessible at the present time. An Initial Scientific Review and Minieconomic Review are conducted simultaneously to determine if there is enough data to make a judgment with respect to the "safety and efficacy" of the substitute chemical. Phase II is only performed if the Phase I reviews identify certain questions of safety or lack of benefits. The Phase II reviews conduct in-depth studies of these questions of safety and cost/benefits and consider both present and projected future uses of the substitute chemicals.

The report summarizes rather than interprets scientific data reviewed during the course of the studies. Data is not correlated from different sources. Opinions are not given on contradictory findings.

This report contains the Phase I Initial Scientific and Minieconomic Review of Captan [N-(trichloromethylio)-4-cyclohexene-1,2-dicarboximide]. Captan was identified as a registered substitute chemical for certain problematic uses of the ethylenebisdithiocarbamate (EBDC) fungicides which are under internal EPA review for suspected adverse effects. Where applicable, the review also identifies areas where technical data may be lacking so that appropriate studies may be initiated to develop desirable information.

The review covers all uses of captan and is intended to be adaptable to future needs. Should captan be identified as a substitute for a problem pesticide other than EBDC fungicides, the review can be updated and made readily available for use. The data contained in this report was not intended to be complete in all areas. Data-searches ended in January, 1975. This review was coordinated by a team of EPA scientists in the Criteria and Evaluation Division of the Office of Pesticide Programs. The responsibility of the team leader was to provide guidance and direction and technically review information retrieved during the course of the study. The following EPA scientists were members of the review team: Eugene Pelletier, Ph.D. (Registered Uses), team leader; Padma Datta, Ph.D. (Chemistry); William Burnam (Pharmacology and Toxicology); John Bowser (Fate and Significance in the Environment); Howard Kerby, Ph.D. (Fate and Significance in the Environment); Jeff Conopask (Economics).

Data research, abstracting and collection were primarily performed by Midwest Research Institute, Kansas City, Missouri (EPA Contract #68-01-2448). RvR Consultants, Shawnee Mission, Kansas, under a subcontract to Midwest Research, assisted in data collection. Stauffer Chemical Company and Chevron Chemical Company, manufacturers of captan, made certain comments and additions to this report. The recommendations of the following National Environmental Research Centers, EPA Office of Research and Development have also been incorporated: Gulf Breeze Environmental Research Laboratory, Gulf Breeze, Florida; National Water Quality Laboratory, Duluth, Minnesota; Southeast Environmental Research Laboratory, Athens, Georgia.

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PART I. SUMMARY

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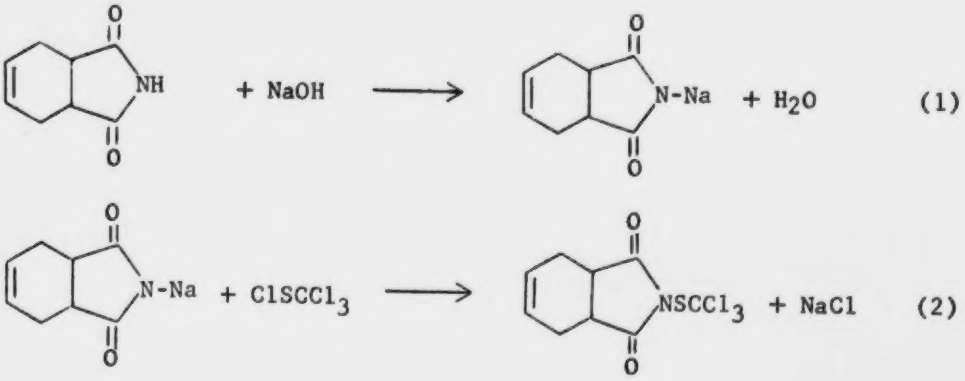
This subsection contains a brief summary of the Initial Scientific and Minieconomic Review conducted on captan. The section summarizes rather than interprets scientific data reviewed.

Production and Use

Captan [N-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide] is a contact fungicide effective against a fairly broad spectrum of plant pathogenic fungi. It is estimated that about 17 million pounds of captan were produced in the United States in 1972 by the only major domestic manufacturer, Calhio Chemicals, Inc., a jointly owned subsidiary of Stauffer Chemical Company and Chevron Chemical Company. The production plant is located in Perry, Ohio.

Captan is manufactured in a two-step synthesis, followed by several purification steps:



Captan

Available literature on the chemistry of captan focuses primarily on degradation reactions. Captan is reported to be decomposed by hydrolysis (essentially complete hydrolysis of a 2% slurry at 100° C in 2-1/2 hr); thermal decomposition; and photolysis.

Captan is available to users in the United States in a great variety of dry formulations, i.e., wettable powders, dusts, and as a 4.0 lb/gal aqueous suspension.

In addition to the products that contain captan as the only active ingredient, a number of formulations (dusts and granulars) are available containing captan in combination with other fungicides and/or insecticides for foliar application and seed treatment. The 50 and 80% wettable powders and 7.5 to 15% dusts that contain captan alone as an active ingredient are apparently the most widely used formulations.

An estimated 16 million pounds of captan were used in the United States in 1972--about 10 to 15 million pounds in agriculture and 1 million by home gardeners. Regional consumption of the captan used for agriculture in 1972 is estimated as follows: Northeastern states--3.5 million pounds (primarily on apples, other deciduous fruits, and small fruits); Southeastern states--2.0 million pounds; North Central states--2.0 million pounds; Northwestern states--1.7 million pounds; South Central states--500,000 pounds; and Southwestern states--300,000 pounds. The use of captan on fruit and nut crops is estimated to account for about 9 million pounds in 1972, i.e., 90% of all the captan used in agriculture.

Toxicity and Physiological Effects

Toxicity - Limited data were found on the acute and subacute toxicity, inhalation effects, or the possible occupational hazards (in manufacture or application) of captan on man. In a study of chromosomal aberrations among workers in a captan formulating plant, no chromosomal damage was reported. Captan is considered to be a mild sensitizer.

The LD_{50} of captan in rats ranges from approximately 8,400 to 12,000 mg/kg of body weight. The chronic oral LD_{50} (100 days) for rats is 916 ± 233 mg/kg body weight per day. Mice have received 560 ppm in the diet for 18 months without any lethal toxic effects.

The "no effect" level of captan for dogs is 100 mg/kg/day (duration of test not specified). Swine have consumed 4,000 ppm of captan over a 175-day period without any toxoic symptoms. In an analysis of pesticide residues in food, the Food and Agricultural Organization/World Health Organization (FAO/WHO) in 1970 reported 12.5 mg/kg as the dose producing no adverse effects for monkeys, after eleven days of dosing.

Cattle and sheep seem to be selectively sensitive to captan: six doses of 250 mg/kg/day caused death in cattle, and sheep have been poisoned by single doses of 250 mg/kg or higher.

Metabolism - Captan is rapidly absorbed from the gastrointestinal tract and is rapidly destroyed in the blood. It does not accumulate in the tissues of pigs or chickens. Captan reacts readily with cysteine, glutathione and other compounds containing SH groups.

Until recently the major metabolic products of captan were considered to be tetrahydrophthalimide (THPI), chloride ion, thiophosgene, carbonyl sulfide, hydrogen sulfide and a substituted thiazolidinethione. Investigators have now found THPI to be further metabolized to 3-OHTHPI, 3-OH-tetrahydrophthalamic acid, THPI-epoxide and 4,5-di-OH-THPI.

Captan induces mitochondrial swelling by two mechanisms, one of which is energy dependent.

Reproduction - Up to 1,000 ppm of captan was fed to two generations of rats (two litters per generation) without any effect on fertility, gestation, viability or lactation indices. In the third generation, the lactation index was suppressed slightly. When captan was given in daily doses of 6 to 57 mg/kg, sperm motility was decreased in rats. The same observation was made for mice (daily dosage 20 to 25 mg/kg). In another test, mice received 50 or 100 mg/kg for 5 days. The fertility index was depressed at the 100 mg/kg level. The weaning weights were decreased in the first litter of the second generation.

Teratology - Single and multiple doses (200 to 1,000 mg/kg) of captan have been given to pregnant hamsters on the 7th and 8th day and on days 6 to 10 of gestation. Anomalies occurred after single-dose administration. A dose level of 750 mg/kg given on day 7 resulted in 13.7% deformed young and 22% mortality among the dams. When a dose of 500 mg/kg was given on days 6 to 10 of gestation, the young were normal. At higher levels fetal death and small fetuses were observed, but there were no anomalies.

In another test, hamsters were given 125, 250 and 1,000 mg/kg of captan each day for the first 15 days of gestation. There were no more terata in the test group that received 1,000 mg/kg than in the control group.

Results of studies on rabbits are contradictory. In two studies, levels of 80 and 75 mg/kg during gestation (7 through 12 days and 6 through 16 days, respectively) produced no malformed fetuses. Conversely, nine malformed fetuses were found in 75 implants in nine pregnant rabbits in another study. In a further investigation, high levels of captan (50 to 2,000 mg/kg body weight) did not produce a significant increase in the number of abnormalities (371 fetuses were observed).

No teratogenic effects were observed in monkeys receiving daily doses of 6.25, 12.5 or 25 mg/kg of captan. Fetal mortality was high at the 25 mg/kg level.

An incidence of 7 to 8% malformations has been observed in chick embryos where the eggs were injected with 3 to 20 ppm of captan. Feeding studies resulted in no terata.

In tissue cultures (human embryonic cells), 4 mg/ml of captan severely inhibited growth for 48 hr. After that period the cells recovered and normal growth ensued.

Mutagenesis - A number of investigations have been made of mutagenic effects of captan. Mutations have been observed in microorganisms, Escherichia coli, Salmonella typhimurium, Neurospora crassa, Saccharomyces cerevisiae. Two hundred fifty micrograms per assay disk of captan in contact with Escherichia coli produced a sixfold increase in mutants; a tenfold increase was produced by 1,000 μg/assay disk.

Captan produced positive evidence of mutagenesis in the forward mutation system and none in the reverse mutation system using Neurospora crassa as a test organism.

In one investigation with Saccharomyces cerevisiae, captan was found to be a weak agent for mitotic gene conversion and did not induce cytoplasmic mutation.

In tests using Escherichia coli B/r ochre auxotrophic mutant, captan has produced marked mutagenic activity by causing an approximate 20-fold increase in numbers of revertents in the excision repair deficient strain and approximately 100-fold increase in the excision repair competent strain.

It has been shown in E. coli strains that a substantial part of the mutagenic activity of captan is due to excisable DNA damage mediated by a volatile breakdown product.

In one investigation, captan did not bring about sex-linked recessive lethal mutations, translocations, or dominant lethal mutations in Drosophila melanogaster. Another investigation reported that captan was not mutagenic (sex-linked recessive lethal test) in Drosophila melanogaster. It was concluded that captan was inactivated before it could reach the germ cells.

Chromosome studies were made of a heteroploid human embryonic cell line exposed to captan. An increase in breaks was noted 24 hr after the addition of captan. The breaks persisted for 24 hr. The breaks were mostly chromatid type. In a kangaroo rat cell line, the percentage of chromosome breaks rose from 10% at 1 µg/ml to 70% at 10 µg/ml of captan.

Captan did not produce dominant lethal mutations when mice were injected intraperitoneally (single) with 3.5 and 7.0 mg/kg of captan. In other investigations with mice, the incidence of dominant lethal mutations was in the normal range.

In another experiment, at the highest dose levels of intraperitoneally (10 mg/kg) or orally (200 mg/kg) administered captan, no dominant lethal mutants were indicated; there were no decreases in total implantations per pregnant female.

Oncogenesis - It was shown that captan injected intraperitoneally (0.15 g/kg for 14 days) increased the mean survival times of mice (26 to 80 days) inoculated with ascites tumor cells 1 day prior to captan treatment. All mice treated with captan developed solid masses at the site of injection into the abdominal wall; no histological evaluations of the masses were made.

Captan has been administered to mice at a level equivalent to about 560 ppm in the diet for 18 months; there was no significant increase of tumors over the controls.

Food Tolerances and Acceptable Intake

Tolerances for captan residues have been established in the United States on 67 raw agricultural commodities. These tolerances range from 2 to 100 ppm. Ten of these 67 tolerances are currently designated as interim. Captan tolerances established by the World Health Organization range from 5 to 40 ppm.

Captan has not been reported as a significant residue in any food crops. Captan residues are detected only occasionally in samples from FDA total diet studies, and analytical tests specifically for captan are not ordinarily performed.

The acceptable daily intake (ADI) for captan was set at the 1965 joint meeting of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues. The ADI for captan is 0.125 mg/kg.

Environmental Effects

The toxicity of captan to fish has been studied in some detail. The effects of captan on other aquatic species, however, have not been as thoroughly examined. Available acute toxicity data for captan to fish are summarized as follows:

Specie	Age	Toxicity calculation	Toxicity measured	System
Fathead minnows	3.5 Months	TL_m (96 hr)	65 μg/ℓ	Flow-through
Fathead minnows	Fingerlings	LC_{50} (96 hr)	120 μg/ℓ	Flow-through
Bluegills	1.5 Months	TL_m (96 hr)	72 μg/ℓ	--
Bluegills	Fingerlings	LC_{50} (96 hr)	150 μg/ℓ	Static
Brook trout	1.5 Months	TL_m (96 hr)	34 μg/ℓ	--
Zebrafish	Larvae	LC_{50} (90 min)	0.67 ppm	--
Carp	Young	TL_m (48 hr)	0.25 ppm	--
Goldfish	Young	TL_m (48 hr)	0.037 ppm	--
Rainbow trout	Fingerlings	LC_{50} (96 hr)	102 μg/ℓ	Static
Coho salmon	Fingerlings	LC_{50} (96 hr)	56.5 μg/ℓ	Flow-through
Lake trout	Fingerlings	LC_{50} (96 hr)	51.0 μg/ℓ	Flow-through
Channel catfish	Fingerlings	LC_{50} (96 hr)	77.5 μg/ℓ	Static
Lake trout	Fingerlings	LC_{50} (96 hr)	75.2 μg/ℓ	Static
Cutthroat trout	Fingerlings	LC_{50} (96 hr)	48.5 μg/ℓ	Static

LC_{50} values for captan in the food of mallard ducks, pheasants, Japanese quail, and bobwhite quail (all 2 weeks old) were found to be > 5,000, > 5,000, > 5,000, and > 2,400 ppm, respectively. Captan is not toxic to red-wing blackbirds and starlings at a single oral dose of 100 mg/kg.

The observations of numerous investigators indicate that captan, at fungicidally effective rates of application, appears to be relatively harmless to beneficial insects (predators and parasites) occurring in deciduous fruit orchards. The review included reports of investigation on the following: Predatory mites (*Thyplodromus* sp., *Amblyseius fallacis*, and *Agistemus fleschneri*), European red mite (*Panonychus ulmi*), larvae of the aphid lion (*Chrysopa carnea*), parasitic wasps (*Trichogramma* sp., *Mormoniella vitripennis*, and *Aphelinus mali*), and predatory bugs (*Anthocoris nemorum* and *Orius* sp.). Among all of the accounts reviewed, only one reported "some mortality" to the predatory bug *Orius* sp., and to the parasitic wasp *Aphelinus mali*. Captan is considered relatively non-toxic to honey bees.

The data reviewed indicates that captan affects a number of soil bacteria and fungi. In tests where captan was applied to cultures of the predominant microfungi of cattail marsh (*Hansenula saturnus*, *Mucor hiemalis*, *Penicillium stipitatum*, and *Trichoderma viride*), all four fungi were inhibited. However, subsequent application of captan to field plots in a cattail marsh did not reduce the number of microfungal propagules in the litter, water or mud.

Field and greenhouse trials showed that captan, at the concentration of 250 ppm, stimulated the soil bacteria in loam soil for about 12 weeks. Actinomycetes were least affected, while most of the physiological groups of the soil bacteria, such as nitrogen-fixing organisms, cellulose decomposers, spore-forming bacteria, and denitrifying bacteria, were stimulated. In some instances, the addition of captan resulted in a decrease in the nitrifying bacteria, ammonifying forms, anaerobic bacteria, and soil algae. *Azotobacter chroococcum* was significantly inhibited for several weeks. Many soil fungi, including *Penicillium*, *Aspergillus*, *Trichoderma*, *Cephalosporium*, *Hyalopus*, *Acrostalagmus*, *Verticillium*, *Aleurisma*, *Sporotrichum*, *Strachybotrys*, *Phymatotrichum*, *Phoma*, *Spicaria*, *Hormodendrum*, *Claddsporium*, *Scopulariopsis*, *Oospora* and *Fusarium* were markedly reduced.

Few reports were found on the toxicity of captan to the lower terrestrial fauna. One review report and several studies on earthworms indicate that captan is relatively nontoxic to such organisms.

Data on the residues of captan in the natural soil indicate that captan appears to be rapidly degraded. Captan is believed to be degradable by biological as well as by chemical mechanisms. When captan is uniformly distributed in the soil, its half-life ranges from 1 to 2 weeks to only 1 to 2 days, depending on a number of environmental factors. When applied to the soil at localized higher concentrations (e.g., seed protectant use), captan residues persist longer in those specific locales. Degradation in a loam soil is reported to be 99% in seven days.

There were no reports found on the presence (or absence) of captan in water, air, or nontarget plants.

A recent study of the bioaccumulation and biomagnification of captan using a terrestrial-aquatic model ecosystem showed that none of the test organisms contained any captan residues at the end of a 33-day test. The investigators concluded that captan does not persist in water, and that "it appears that continued use of captan will not have any serious environmental impact, as it does not persist in the water of this 33-day model ecosystem, nor does it accumulate in the fish which is the upper member of the food chain."

Available data indicates that captan is rapidly degraded by chemical as well as by biological mechanisms. Captan has been rated using an index designed to determine the propensity of pesticides for volatilization and leaching under simulated field conditions for loam soils at 25° C and an annual rainfall of 59 in. By this method, captan rated a volatilization index of 2, indicating an estimated median vapor loss from treated areas of 1.8 lb/acre/year. This index number indicates that the propensity for volatilization of captan from treated fields is in the intermediate range, compared to other pesticides. Captan rated a leaching index number of 1, indicating movement of less than 4 in. through the soil.

Limitations in Available Scientific Data

The review of scientific literature was based on available sources given limitations of time and resources. Data was not found in a number of pertinent areas:

1. LD_{50} values for intravenous, subcutaneous, and intraperitoneal injection in various species.
2. Inhalation toxicity. Studies should be conducted on application rates, modes of spray application and spraying conditions to the inhalation exposure experienced by workers.
3. Laboratory and field studies on effects on lower aquatic organisms.
4. Residues in water and air.

Efficacy and Cost Effectiveness

The economic benefits of using captan have been determined from field tests for control of scab and rot on apples; brown rot and scab on peaches; gray mold of strawberries, potato scab on potatoes; and seedling diseases of soybeans. However, the data is incomplete and should be looked upon with caution.

Captan is a good all-around fungicide for control of scab and rots on apples. Although several tests have been reported in which yields of captan treated trees were measured, none compared to the test results untreated trees. Since apple crops are greatly reduced when no fungicide is used, the yields from these trees were used as a direct measure in estimating economic benefits.

Captan also controls brown rot and improves the finish of ripened peaches. The results of one set of tests showed a 42 lb/tree increased yield due to the use of captan. This resulted in an economic benefit of $2.60/tree.

Potato seeds treated with captan for potato scab have shown yield increases ranging from 15 to 58 cwt/acre. The resultant economic benefits varied from $35.60 to $142.50/acre.

Soybean seedlings treated with captan resulted in a 3.7 bushel yield increase in a test in Tennessee. This result, which may not be typical, demonstrates an economic benefit of $12.90/acre.

More detailed data on the efficacy and cost effectiveness of captan on apples and strawberries appears in Part III.

PART II. INITIAL SCIENTIFIC REVIEW

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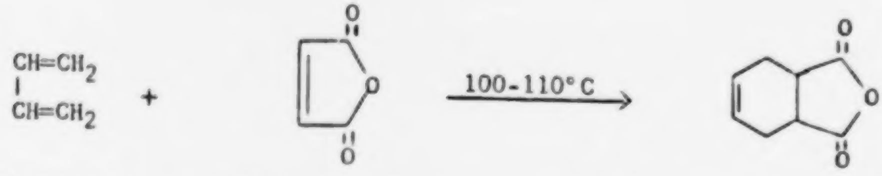
This section contains a detailed review of available data on captan's chemistry and presence in foods. Eight subject areas have been examined: Synthesis and Production Technology; Physical Properties of Captan; Analytical Methods; Composition and Formulation; Chemical Properties, Degradation Reactions and Decomposition Processes; Occurrence of Residues in Food and Feed Commodities; Acceptable Daily Intake; and Tolerances. The section summarizes rather than interprets data reviewed.

Synthesis and Production Technology

The only major manufacturer of captan in the U.S. is Calhio Corporation, a jointly owned subsidiary of Stauffer Chemical Company and Chevron Chemical Company (part of Standard Oil of California). Their plant is located in Perry, Ohio, has annual capacity of 25 million pounds per year, and is also used for manufacturing folpet, an analog of captan.

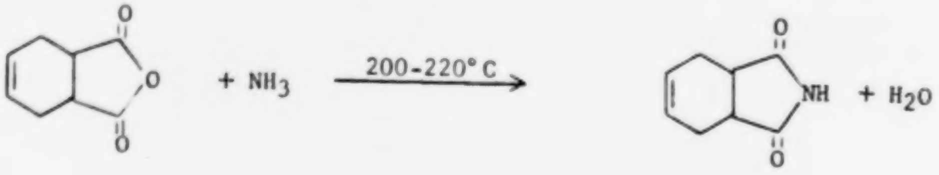
Captan is made in a two-step reaction process followed by several purification steps. The process uses two intermediates which are manufactured on site.

One of these intermediates is tetrahydrophthalimide, which is also made by a two-step reaction:



(1)

Butadiene Maleic anhydride Tetrahydrophthalic anhydride

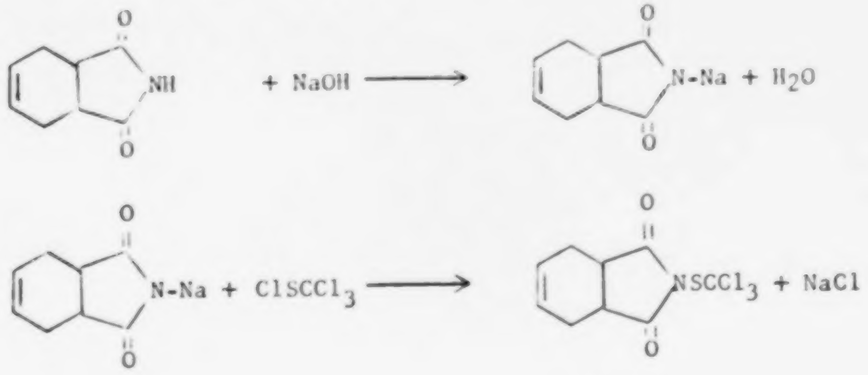


(2)

The second intermediate is perchloromethyl mercaptan, made by the following reaction:

$$CS_2 + 3Cl_2 \xrightarrow{I_2} CCl_3SCl + SCl_2 \qquad (3)$$

The tetrahydrophthalimide is mixed with sodium hydroxide then reacted with perchloromethyl mercaptan as follows:



(4)

(5)

Captan

The schematic diagram for the production of captan by Calhio is shown in Figure 1.

Reaction (1) proceeds smoothly with a minimum of by-product. The anhydride is typically above 99% purity and contains minute quantities of vinyl cyclohexene and other butadiene polymeric materials as the major impurities (California Spray-Chemical Corporation, 1955)[1]. The reaction is carried out by bubbling butadiene gas into molten maleic anhydride at a temperature of 100 to 110°C (Kittleson, 1953)[2].

In Reaction (2), a small amount of colored maleimide resin polymers are formed from the reaction of ammonia and unreacted maleic anhydride. The reaction is run at a high temperature to boil off the water, and, during this process, all of the vinyl cyclohexene and most of the other volatile impurities are removed. The purity of the imide is typically 98% with residual water and tetrahydrophthalic anhydride being the major impurities (California Spray-Chemical Corporation, 1955).

Reaction (3) to produce perchloromethyl mercaptan is performed at 0 to 15°C. The pressure is approximately atmospheric or slightly higher. The reaction is exothermic. Iodine is a common catalyst, but ferric chloride or aluminum chloride may be used (Sittig, 1967)[3]. The final purity is 96% purity or better (California Spray-Chemical Corporation, 1955).

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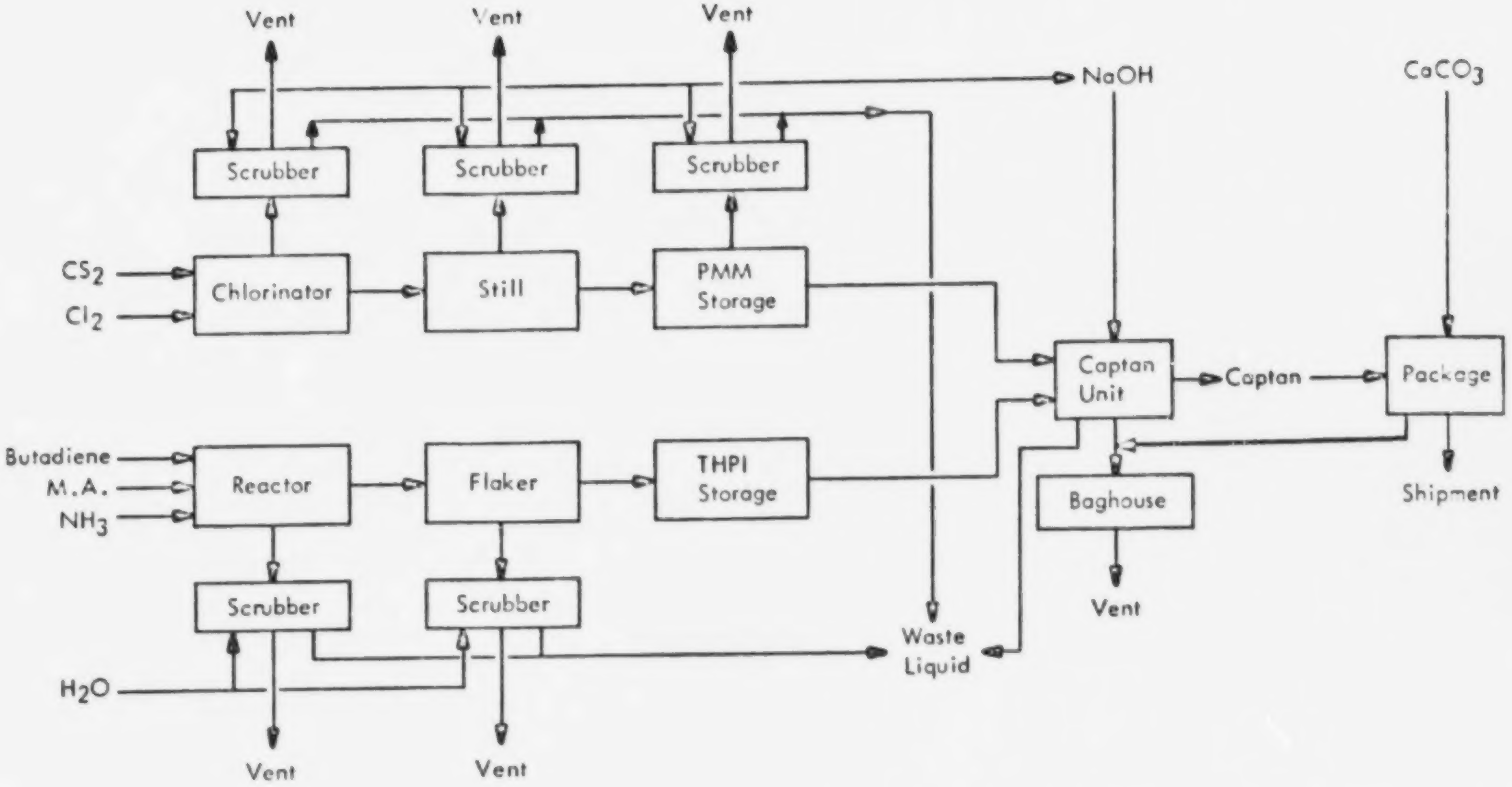
[1] California Spray-Chemical Corporation, The Chemistry of Captan, Kansas City, Mo. (31 March 1955).

[2] Kittleson, A. R., "Preparation and Some Properties of N-Trichloromethylthiotetrahydrophthalimide," J. Agr. Food Chem., 1(10):667-679 (5 August 1953).

[3] Sittig, M., Pesticide Production Processes, Chemical Process Review No. 5, Park Ridge, New Jersey, Noyes Development Corporation (1967).


Vent
Vent
Vent
Scrubber
Scrubber
Scrubber
NaOH
CaCO$_3$
CS$_2$
Cl$_2$
Chlorinator
Still
PMM Storage
Captan Unit
Captan
Package
Butadiene
M.A.
NH$_3$
Reactor
Flaker
THPI Storage
Baghouse
Shipment
Scrubber
Scrubber
Vent
H$_2$O
Waste Liquid
Vent
Vent

Source: Lawless, E. W., and T. L. Ferguson of Midwest Research Institute, and R. von Rümker of RvR Consultants, The Pollution Potential in Pesticide Manufacturing, for the Environmental Protection Agency, Contract No. 68-01-0142 (January 1972).

Figure 1. Production and waste schematic for captan.

Reaction (4) is a simple mixing-dissolving step.

Reaction (5) (captan production) is controlled at a temperature between 10 and 30°C, preferably about 20°C, and at essentially atmospheric pressure. Reaction time is from 10 to 40 min. The reaction is carried out in an aqueous medium of pH 10.0 to 10.5. No catalyst is used (Sittig, 1967). The pH must be kept as low as possible to prevent decomposition of the product, but high enough to drive the reaction to completion by absorbing the HCl formed.

Kittleson and Nelson (1958)[1] in a U.S. patent describe how the reaction may be carried out in an inert organic solvent. Possible solvents include ketones, aromatic, aliphatic or chlorinated hydrocarbons. A tertiary amine is used to absorb the HCl formed in the reaction.

Kittleson and Yowell (1951)[2] report yields of 85 to 95% in captan manufacture.

Table 1 presents a list of raw materials and process wastes and losses.

Physical Properties of Captan

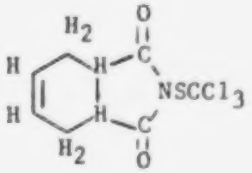
Chemical Name: N-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide.

Common Name: Captan

Trade Names: Merpan, Orthocide, SR-406, Vancide.

Pesticide Class: Fungicide; Chlorinated organosulfur compound.

Structural formula:



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[1] Kittleson, A. R., and J. F. Nelson (to Esso Research), U.S. Patent 2,856,410 (14 October 1958).

[2] Kittleson, A. R., and H. L. Yowell (to Standard Oil Development Company), U.S. Patent 2,553,771 (22 May 1951).

Table 1. RAW MATERIALS AND BY-PRODUCTS IN THE MANUFACTURE OF CAPTAN

Raw materials

Material	Received from	Received by	Storage
1. CS_2	Delaware	Tank cars	
2. I_2	Michigan	Drums	Drums
3. Cl_2	Louisiana	Tank cars	Used directly from tanks
4. NH_3	West Virginia, Kentucky	Tank cars	Used directly from tanks
5. $CaCO_3$		Truck loads	Bulk
6. Maleic anhydride	Missouri, Pennsylvania, New Jersey	Tank cars	
7. Butadiene	Texas	Tank cars	
8. NaOH		Tank cars	

Process Wastes and Losses

Material	Form	Amount produced (lb/lb AI)	Disposition
1. Active ingredient	Particulates	Approximately 4 Lb/day	
2. Solvents			
3. Liquid		10 Tons/year	Asphalt lined settling pond; discharge
4. Solid paper		10 Tons/year	Local collector
5. Metal		25 Tons/year	Local scrap dealers
6. Miscellaneous chemicals		1,200 Lb/year	Buried on plant property

Source: Lawless et al., *op*. *cit*. (1972).

Empirical Formula: $C_9H_8Cl_3NO_2S$.

Molecular Weight: 300.61.

Analysis: C, 35.96%; H, 2.69%; N, 4.67%; Cl, 35.50%; S, 10.67%; O, 10.65%.

Physical State	Pure	Technical
	White crystals	Yellow to buff colored amorphous powder
Odor:	Odorless	Pungent
Melting Point:	178°C (Martin, 1971)[1]	160-170°C (Martin, 1971)
	174-176°C (Stauffer, 1965)[2]	
	172-173°C (Merck, 1968)[3]	158-164°C (Stauffer, 1965)
Boiling Point:	Decomposes near melting point.	
Specific Gravity (20/20°C):	1.73	1.62
Bulk Density:		25-30 lb/ft^2

Vapor Pressure: 6×10^{-5} mm Hg at 25°.

pH: 8.0-8.3 Typical (electrometric, 10% dispersion in water).

Particle Size: 9-13 μ Surface average diameter by air permeation.

Captan Content in Technical Product (Stauffer, 1965): 92% Typical. Seldom less than 90% or more than 94%.

Noncaptan Chlorine (Stauffer, 1965): Analysis by chlorine content typically gives results almost 2% too high when calculated as captan.

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[1] Martin, H., Pesticide Manual, British Crop Protection Council, 2nd ed. (1971).

[2] Stauffer Chemical Company, "Technical Captan," (Data Sheet) (1965).

[3] Merck Index, The, P. G. Strecher (Ed.), 8th ed., Rahway, New Jersey: Merck and Company (1968).

Solubility of Captan in Various Solvents (Stauffer, 1965):

Substance	Grams/100 ml of solvent (25°C)	Other temperatures
Tetrachloroethane	8.15	
Chloroform	8.0	
Xylene	6.5	
Dioxolane	5.0	
Cyclohexanone	4.96	10 at 77°C, 20 at 88°C
Dioxane	4.7	20 at 91°C
Ethyl acetate	4.5	9 at 74°C
Benzonitrile	4.0 (12°)	15 at 50°C
Acetonitrile	3.6 (22°)	9.1 at 50°C
Chlorobenzene	3.3	10 at 61°C
Methyl chloride	3.0	
Acetone	3.0	9 at 57°C
Ethylene chloride	2.85	20 at 80°C
Nitromethane	2.0	10 at 84°C
Velsicol AR-50	Less than 2	4.5 at 50°C
Benzene	1.8	10 at 78°C
Isopropyl alcohol	0.8	6 at 81°C
Toluene	0.7	10 at 90°C, 20 at 105°C
Methyl alcohol	0.5	5 at 60°C
Ethanol	0.29	
Diethyl ether	0.25	
Heptane	0.04	
Stove oil		Less than 1% at 70°C
Carbitol		Less than 1% at 60°C
Water[a]	Less than 0.5 ppm	

---

[a] Ortho Technical Information, Chevron Chemical Company (April 1974), stated that the solubility in water at 25°C is 3.3 ppm.

Analytical Methods

This subsection reviews captan's analytical methods and the most significant of many primary information sources on the methods. The following information sources are described: (1) Pesticide Analytical Manual (PAM), vols. I, II,[1] (2) Official Methods of Analysis of the Association of Official Analytical Chemists,[2] (3) Analytical Methods for Pesticides and Plant Growth Regulators.[3]

The Pesticide Analytical Manual - The "Pesticide Analytical Manual" (PAM) is published by the Food and Drug Administration, for the purpose of bringing together procedures and methods used by the FDA laboratories to examine food samples for the presence of pesticide residues. The PAM is published in two volumes. Volume I contains procedures for multi-residue methods (for samples of unknown history which may contain more than one pesticide). Volume II contains analytical methods used for specific pesticide residues and for specific foods.

Official Methods of Analysis of the Association of Official Analytical Chemists - The Association of Official Analytical Chemists (AOAC) publishes an authoritative manual of "Methods of Analysis." A new edition of this manual is published about every 5 years. The reliability of the methods must be demonstrated by a published study showing the reproducibility of the method by professional analysts. Methods and collaborative studies are published in the Journal of the Association of Official Analytical Chemists.

Analytical Methods for Pesticides and Plant Growth Regulators, Volume VI, Gas Chromatographic Analysis - This text (Zweig and Sherma, 1972) contains valuable information concerning gas chromatographic analytical techniques. It provides a review of literature concerned with formulation and residue analyses for captan.

Multi-Residue Methods -

Multi-residue methods for captan are described in PAM, Volume I. Zweig and Sherma (1972) have compiled a detailed review of gas chromatographic residue analyses. AOAC multi-residue methods are not applicable to captan.

1/ U.S. Department of Health, Education, and Welfare, Food and Drug Administration, Pesticide Analytical Manual, 2 vols. (1971).

2/ Association of Official Analytical Chemists, Official Methods of Analysis of the Association of Official Analytical Chemists, 11th ed., Washington, D.C. (1970).

3/ Zweig., G, and J. Sherma, Analytical Methods for Pesticides and Plant Growth Regulators, Vol VI: Gas Chromatographic Analysis, Academic Press, New York (1972).

PAM Procedures - The PAM multi-residue methods apply to the wide variety of foods tested by the FDA. However, the multi-residue methods are not capable of detecting and measuring all pesticides. Analytical schemes specified for the detection of captan are shown in Figures 2 and 3. The various parts of the schemes shown in Figures 2 and 3 are outlined in detail in the PAM. (The numbers refer to the chemical numbering system of PAM; the chapter numbers also refer to PAM.)

From conferences with FDA officials, it was learned that the analytical system used by the FDA laboratories (in Kansas City) does detect captan. However, the recoveries are low (about 50%) because analytical response is not good (detection of captan by the gas chromatographic procedure is somewhat erratic). However, captan residues are detected only occasionally in the total diet studies and specific analysis for captan is not routinely made by the FDA.

A major difficulty appears to be the erratic recovery of captan by the extraction and cleanup procedure. PAM states that data is unavailable on the recovery of captan from fatty foods. In the analysis of nonfatty foods, captan is not recovered in either the 6% or 15% fraction (ethyl ether in petroleum ether) from the Florisil column. (See PAM Table 20-A). PAM Table 201-G notes that Eluant C (50% methylene chloride, 1.5% acetonitrile and 48.8% hexane) is suitable for captan.

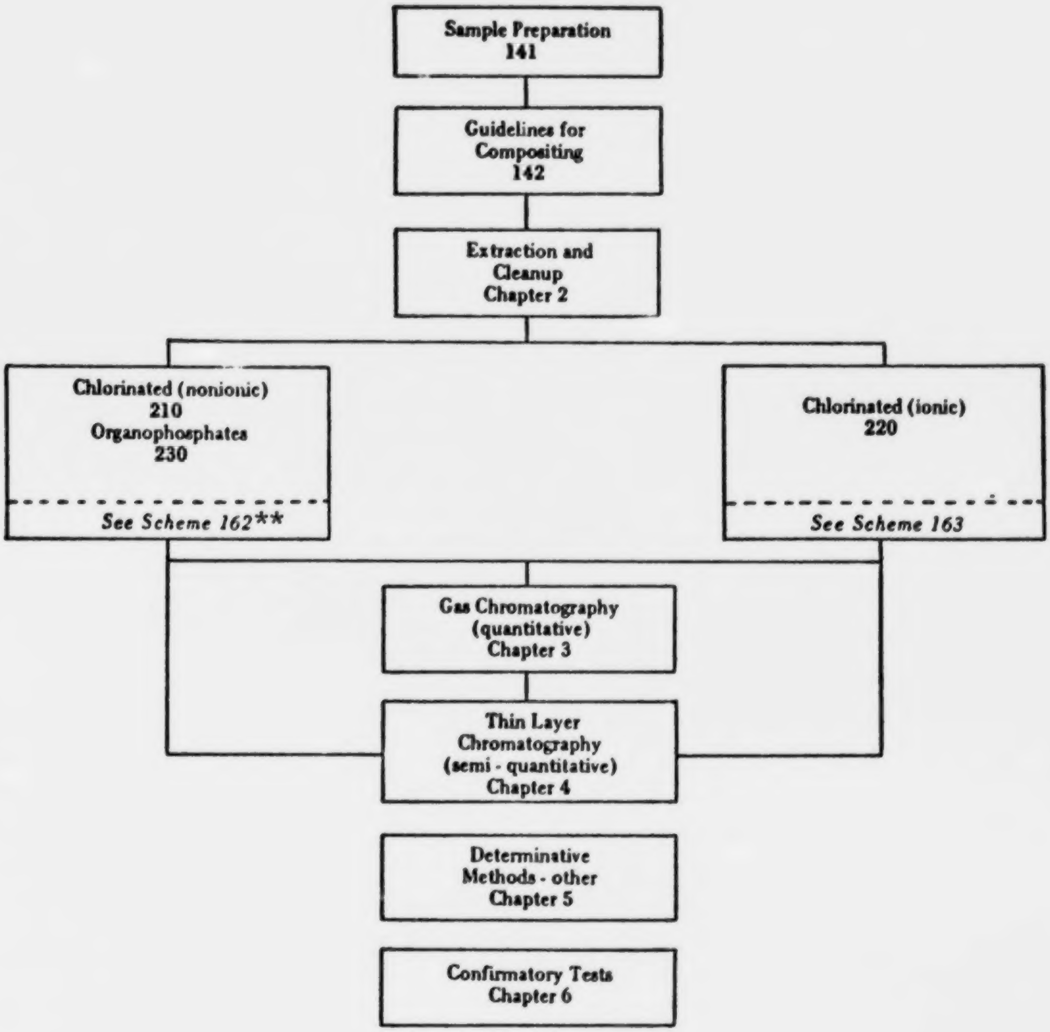
Relative retention times of captan are presented below for various column packings; the corresponding response for various detectors is also indicated.

Residue Analysis Principles -

Both the AOAC methods manual and PAM (Vol. II) describe methods for the specific analysis of captan residues. Zweig and Sherma have provided a review of specific residue analytical methods for captan.

AOAC Method (Official Final Action) - According to the AOAC method for specific analysis of captan residues, captan is extracted with benzene. Water, colored materials, and appreciable amounts of waxes are removed from the benzene solution using a cleanup mix (a mixture of Nuchar, Hyflo Super-Cell and anhydrous sodium sulfate). A red color is developed by fusion of captan with resorcinol (after evaporation) at 135°C. This color changes to yellow on addition of acetic acid. The concentration of captan is determined spectrophotometrically at 425 µm using a standard reference curve.

The method is applicable to firm fruits such as apples, pears, peaches, and plums and to green vegetables.

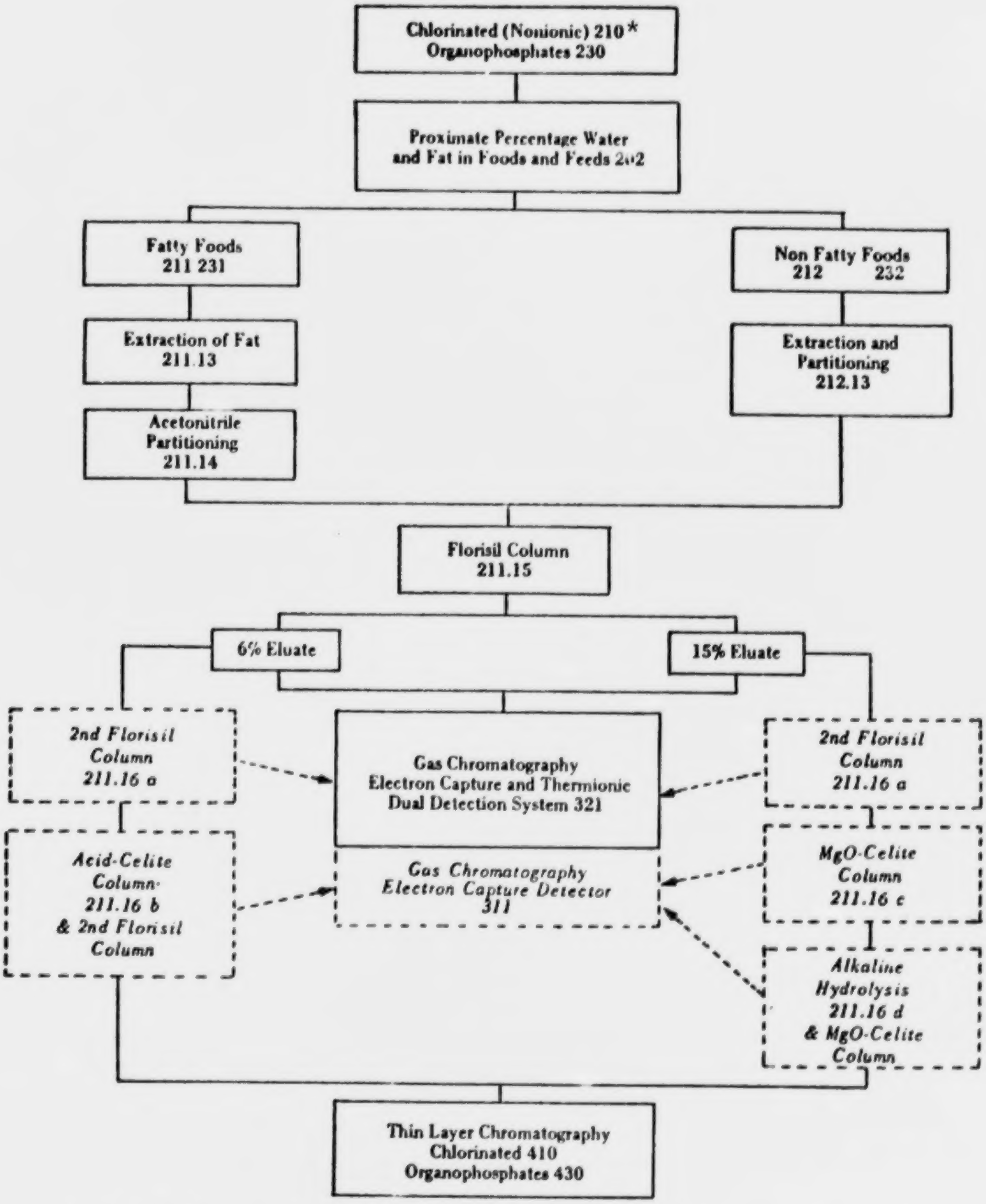

Sample Preparation
141
Guidelines for Compositing
142
Extraction and Cleanup
Chapter 2
Chlorinated (nonionic)
210
Organophosphates
230
See Scheme 162**
Chlorinated (ionic)
220
See Scheme 163
Gas Chromatography (quantitative)
Chapter 3
Thin Layer Chromatography (semi - quantitative)
Chapter 4
Determinative Methods - other
Chapter 5
Confirmatory Tests
Chapter 6

* The numbers refer to the decimal numbering system of PAM. Chapter numbers also refer to PAM.

** Scheme 162 is presented in Figure 2.

Source: PAM (1971).

Figure 2. General scheme for multiple residues*


Chlorinated (Nonionic) 210*
Organophosphates 230
Proximate Percentage Water and Fat in Foods and Feeds 202
Fatty Foods 211 231
Non Fatty Foods 212 232
Extraction of Fat 211.13
Acetonitrile Partitioning 211.14
Extraction and Partitioning 212.13
Florisil Column 211.15
6% Eluate
15% Eluate
2nd Florisil Column 211.16 a
Gas Chromatography Electron Capture and Thermionic Dual Detection System 321
2nd Florisil Column 211.16 a
Acid-Celite Column 211.16 b & 2nd Florisil Column
Gas Chromatography Electron Capture Detector 311
MgO-Celite Column 211.16 c
Alkaline Hydrolysis 211.16 d & MgO-Celite Column
Thin Layer Chromatography
Chlorinated 410
Organophosphates 430

* The numbers refer to the decimal numbering system of PAM. The primary analytical scheme is in bold type. Additional cleanup and/or quantitation schemes are in italics.

Source: PAM (1971).

Figure 3. Analytical Scheme for Chlorinated (nonionic) and Organophosphate Residues

Electron Capture Detector

Column packing	Retention time relative to aldrin (ratio)	Response (ng for 1/2 FSD[a] at 1 x 10^{-9} AFS[b])
10% DC 200 on Gas-Chrom Q (or Anakrom Q)	1.22	40-50
15% QF-1, 10% DC 200 on Gas-Chrom Q	2.10	4

Halogen Detector

Column packing	Retention time relative to sulphenone (ratio)	Response (µg for 1/2 FSD[a] 64 ohms)
10% DC 200 on Gas-Chrom Q	1.16	3.5
15% QF-1, 10% DC 200 on Gas-Chrom Q	2.03	3

Sulfur Detector

Column packing	Retention time relative to sulphenone (ratio)	Response (µg for 1/2 FSD[a] 64 ohms)
10% DC 200 on Gas-Chrom Q	0.95	6
15% QF-1, 10% DC 200 on Gas-Chrom Q	0.80	6

---

[a] FSD = Full scale deflection.

[b] AFS = Amps, full scale.

PAM Methods - PAM (1971) lists three methods for specific residue analysis. The first two methods have been "tested in varying degrees and are considered reliable without further validation for the product applications indicated." The third method has not been "thoroughly tested through inter-laboratory studies."

The First Method - This method is a procedure for the determination of captan, folpet and difolatan in crops. The crop sample is extracted with acetonitrile and partitioned into Eluant C. Further cleanup is effected on a Florisil column utilizing two different solvent systems. The pesticide residue is measured by gas chromatography using an electron capture detection system.

Chlorinated insecticides are eluted in the first eluate (20% methylene chloride in petroleum) and captan, folpet and difolatan in the second (50% methylene chloride in petroleum ether). Additional confirmation of the residues can be made using a different column and thin-layer chromatography.

Captan recoveries of 84 to 118% have been obtained on cabbage, carrots and soybeans fortified at 2 ppm level. The procedure can be applied to a variety of raw agricultural commodities. The sensitivity is 0.1 ppm. (Additional information concerning this method is presented in the section on "Other Methods.")

The Second Method - This method refers to the AOAC procedure, described earlier. The sensitivity is 10 ppm. This method, however, does not distinguish between captan and folpet; it may now be obsolete in view of GLC (gas liquid chromatography) methods.

The Third Method - This method (Archer and Corbin, 1969)1/ employs a thin-layer chromatographic technique to detect captan residues in the presence of difolatan residues. The method can selectively detect 1 µg of captan. The sample residue, after extraction from the crop material, is spotted on a Silica Gel H plate. Detection is with either resorcinol, glacial acetic acid or tetraethylammonium hydroxide-pyridine spray reagents.

Other Methods - Zweig and Sherma have reviewed several other residue analysis methods for captan. Kilgore et at. (1967)2/ reported a rapid procedure for determining captan residues on apricots, peaches, tomatoes, and cottonseed. The residues are extracted with benzene or acetonitrile and analyzed by

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1/ Archer, T. E. and J. B. Corbin, "Detection of Captan Residues in Prune Fruits and Blossoms by Thin-Layer Chromatography," Bull. of Environ. Contam. and Toxicol., 4(1):53-63 (1969).

2/ Kilgore, W. W., W. Winterlin, and R. White, "Gas Chromatographic Determination of Captan Residues," J. Agr. Food Chem., 15(6):1035-1037 (1967).

electron capture gas chromatography. Residues as low as 0.01 ppm were detected, and an overall average recovery of captan residues obtained from fortified control samples was 92%.

Bevenue and Ogata (1968)[1/] reported the use of a gas chromatography method for the separation of phaltan (retention = 4.2 min) and captan (5.2 min). Recoveries of the fungicides from fresh papayas fortified at the 1.0 ppm level ranged from 85 to 95%. The procedure involved cleanup of a benzene extract by a 5 min contact with Nuchar-190 carbon.

Pomerantz et al. (1970)[2/] determined captan, phaltan, and difolatan in crops using gas chromatography with electron capture detection. The procedure involved acetonitrile extraction, partitioning into methylene chloride-petroleum ether, and cleanup on Florisil. Recoveries were 80 to 110% for six food crops fortified at levels from 2.0 to 0.1 ppm. The method of Pomerantz et al., is essentially the method used by PAM. None of the GLC methods have been subjected to a full collaborative study.

Formulation Analysis Principles -

A formulation analysis procedure for captan is described in the Journal of the AOAC (Anon., 1971)[3/]. Zweig and Sherma (1972) have provided a review of two other methods. The Technical Service Division of EPA uses the AOAC method and the "Hydrolyzable Chlorine" method.

AOAC Method (Official First Action) - According to a change in AOAC method (Anon., 1971) captan is extracted from inerts with a solution containing dieldrin (as internal standard) in dioxane. The mixture is analyzed using any gas chromatography system which will completely separate captan from dieldrin (under specified conditions, which include a thermal conductivity or hydrogen flame detector). The ratio of captan peak height to dieldrin peak height is measured and compared to the ratio from standard captan prepared similarly. It is not completely satisfactory for all samples, probably due to a tendency of captan to decompose on the GLC column. It has not yet been given official final action.

This method applies to technical and dry formulated products containing captan as the only active ingredient.

[1/] Bevenue, A. and J. N. Ogata, "The Examination of Mixtures of Captan and Phaltan by Gas Chromatography," J. Chromatogr., 36(4):529-531 (Sept. 1968).

[2/] Pomerantz, I. H., L. J. Miller, and G. Kava, "Extraction, Cleanup, and Gas-Liquid Chromatographic Method for the Analysis of Captan, Folpet, and Difolatan in Crops," J. Assoc. Offic. Anal. Chem., 53(1):154-157 (1970).

[3/] "Captan (N-Trichloromethylthio)-4-cyclohexene-1,2-dicarboximide) - Official First Action, J. Assoc. Offic. Anal. Chem., 54(2):451 (1971).

Gas Chromatographic Method - A method recommended by Zweig and Sherma employs a sample of captan (or phaltan) dissolved in acetone. The sample is injected into a gas chromatograph (thermal conductivity detector) and the quantity of captan in the sample is determined by comparing the area of the sample peak with that from a sample of known composition.

Hydrolyzable Chlorine Method - Zweig and Sherma also review an older method based upon the selective hydrolysis of captan followed by halide determination. The method is described by Ospenson, et at. (1964)[1] in Vol. III of Zweig's text, Analytical Methods for Pesticides, Plant Growth Regulators and Food Additives. The method is suitable for the assay of both captan and phaltan and is based on measuring the hydrolyzable chlorine in captan. The method is basically designed for 100% captan, although with proper care it could be adapted for high concentration captan formulations. Materials containing hydrolyzable chlorine interfere. The chloride is measured using the Volhard method on the sample before and after hydrolysis, and the difference calculated to equivalent captan.

Other Methods - The use of liquid chromatography for analysis of captan formulations offers considerable promise. An infrared method has also been used to determine captan in formulation.[2] Bromoform or chloroform is used as a solvent and absorbance is measured at 7.91 microns.

Composition and Formulation

Technical captan is about 92% pure product, the remainder consisting of sodium chloride, water and unreacted tetrahydrophthalimide (FAO/WHO, 1970)[3].

Captan is physically and chemically compatible with practically all common and important agricultural pesticides and formulation materials with the notable exception of alkalies.

Among the alkaline materials, hydrated lime specifically can cause loss of fungicidal activity. Ground limestone, on the other hand, is quite safe and can be used in dry mixtures.

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[1] Ospenson, J. N., D. E. Pack, G. K. Kohn, H. P. Burchfield and E. E. Storrs, "Captan," p. 7, Chapter 2 in Analytical Methods for Pesticides, Plant Growth Regulators and Food Additives, Vol. III, Fungicides, Nematocides and Soil Fumigants, Rodenticides and Food and Feed Additives, Academic Press, New York, New York (1964).

[2] Collaborative International Pesticide Analytical Council, CIPAC Handbook, Vol. I, W. Heffer and Sons, Ltd., Cambridge, pp. 172-183 (1970).

[3] FAO/WHO, Food and Agricultural Organization of the United Nations/World Health Organization, "1969 Evaluations of Some Pesticide Residues in Food," The Monographs, Geneva (1970).

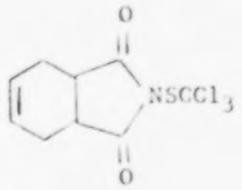
Among the diluents and carriers, all the common types have been used with captan in a variety of applications with good results. For mixtures with insecticides and other fungicides, diluents such as talc, prophyllite and sericite are favored for best results. In sensitive applications where phytoxicity may be a problem, kaolinite diluents may show some activity with captan and should be tested before adoption.

Captan can be used with moderate amounts of oil or other liquids in most applications. However, excessive oil or solvent liquids capable of carrying the fungicide into plant tissues can cause injury in certain applications (Stauffer, 1965).

Formulations of captan available from the manufacturer include: Orthocide 50W (wettable powder containing 50% captan by weight) and Orthocide 80W (wettable powder containing 80% captan by weight). A wide selection of dusts are available, and several formulations of seed protectants are available.

Chemical Properties, Reactions and Decomposition Processes

Captan is chemically classified as a chlorinated organosulfur compound. The technical product is about 92% pure captan. Several chemical names have been used in the past. It was originally called N-trichloromethylthiotetrahydrophthalimide. Chemical Abstract Services (CAS) for a while used the name N-trichloromethylthio-4-cyclohexene-1,2-dicarboximide. This is one of the names approved for use on labels by EPA (Caswell et al., 1972)[1]. CAS now uses the name 3a,4,7,7a-tetrahydro-2-[(trichloromethyl)thio]-1H-isoindole-1,3(2H)-dione. The structure of captan and several of its analogs, which are also used as fungicides, is presented in the following diagram:



Captan

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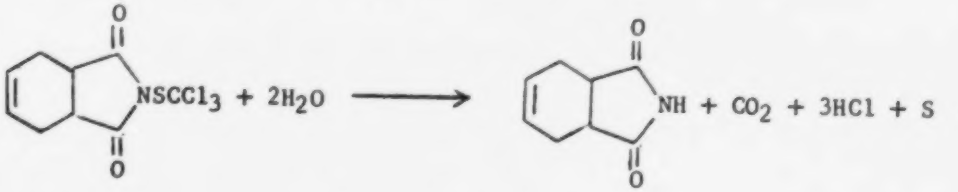
[1] Caswell, R. L., D. E. Johnson, and C. Fleck, "Acceptable Common Names and Chemical Names for the Ingredient Statement on Pesticide Labels," (2nd ed.), Environmental Protection Agency, Washington, D.C. (June 1972).

Kittleson (1953), who obtained the original patent for captan, prepared 17 other compounds containing the N-trichloromethylthio group and found them all to be highly active fungicides. He concluded that the N-trichloromethylthio group was the active portion of the molecule, but, according to Metcalf (1971),[1] this conclusion may be an over-simplification, because the interaction of the molecule with the fungus appears to be a highly complex process (see "Reactions with Thiols," p. 29).

Hydrolysis Reactions - The rate of hydrolysis of captan increases with increasing temperature and increasing alkalinity. The reaction is given by Melnikov (1971)[2] as follows:



(6)

Captan

Tetrahydrophthalimide

This reaction is consistent with the observations of Miller (1957),[2] who suggested the formation of HCl because of the drop in pH from 7.0 to 4.2 when a captan suspension in water was held for 2 weeks at 25°C. He also used $AgNO_3$ to prove that free chloride ions were formed. Daines et al. (1957),[3] however, observed that H_2S is also formed. These investigators used chloride ions and H_2S as criteria of captan decomposition.

The rate of hydrolysis with temperature was studied extensively by Daines et al. (1957). They found that decomposition of a 2% slurry in water occurred rather slowly at temperatures below 110°F, but at 110°F hydrolysis was very rapid. California Spray-Chemical Corporation (1955) held a 2% slurry at 100°C and observed that the hydrolysis was essentially complete in 2-1/2 hr. They gave the chemical reaction as:

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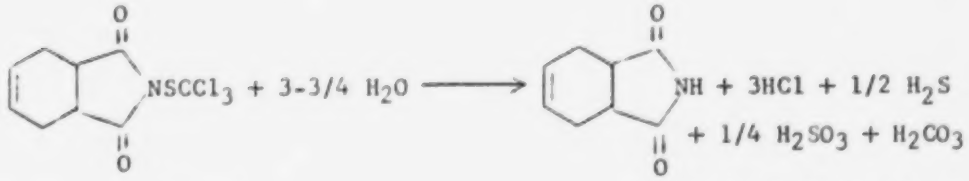
[1] Metcalf, R. L., "Chemistry and Biology of Pesticides," Pesticides in the Environment, R. White-Stevens (ed.), New York, Marcel Dekker, Inc. (1971).

[2] Melnikov, N. N., Chemistry of Pesticides, 36 of Residue Rev., Springer-Verlag, New York, p. 247 (1971).

[3] Daines, Robert H., R. J. Lukens, E. Brennan, and I. A. Leone, "Phytotoxicity of Captan as Influenced by Formulation, Environment, and Plant Factors," Phytopathology, 47(9):567-572 (September 1957).

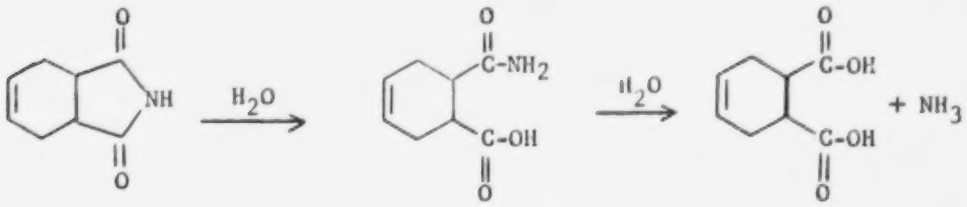


(7)

Captan

Tetrahydrophthalimide

This publication also noted that tetrahydrophthalimide will hydrolyze further according to Equation (8):



(8)

The effect of pH on hydrolysis is very pronounced. Daines et al. (1957) found that there was little captan decomposition at pH 7.0, very rapid decomposition at pH 10.6, and nearly instantaneous decomposition at pH 14. von Rümker and Horay (1972)[1/] gave the following values for hydrolytic stability at various temperature and pH's:

pH	Buffer	Half-life	
		20° C	40° C
4	Acetate	32.4 hr	5.3 hr
7	Citrate	8.3 hr	2.1 hr
10	Carbonate	< 2 min	< 2 min

[1/] von Rümker, R., and F. Horay, Pesticide Manual, Vol. I., Department of State, Agency for International Development (1972).

Thermal Decomposition - von Rümker and Horay (1972) state that dry captan is stable to heat but aqueous suspensions are quickly decomposed at 100°C or in alkaline media. The following thermal stabilities for dry captan are given:

Half-life at 80°C	213 weeks
Half-life at 120°C	14-1/4 days

At temperatures above the melting point (170°C) dry captan is rapidly decomposed.

Pyrolysis of captan by dry distillation at 200°C results in the formation of thiophosgene, tetrahydrophthalimide and "other related products" (California Spray-Chemical Corporation, 1955).

Photolysis Reactions - Lloyd Mitchell (1961)[1] of the FDA subjected many pesticides to ultraviolet radiation of wavelength 253.7 nm. The pesticides were spotted on chromatographic paper and exposed to the radiation for a total of 1 hr. Captan was classified in the category of "degradation complete or practically so." Products were not identified.

However, California Spray-Chemical Corporation (1955) reports that captan is stable to ultraviolet light. Thin layers of recrystallized captan were exposed for 24 hr to a 100 W H-6 mercury lamp. The samples were held at 35°C and purity was checked by melting point and confirmed by biological assay.

Reactions with Thiols - Thiol compounds react with captan and destroy its fungitoxicity (Lukens and Sisler, 1958)[2]. Reactions between captan and thiol groups are believed to be the chemical basis for the fungicidal activity of captan.

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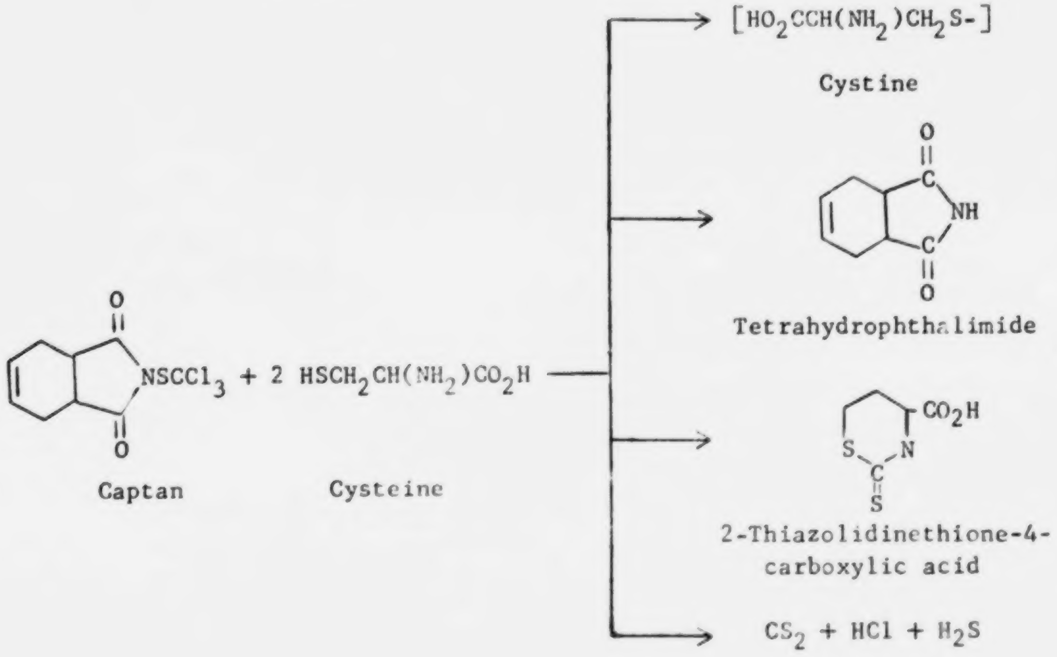
[1] Mitchell, Lloyd C., "The Effect of Ultraviolet Light (2537 A) on 141 Pesticide Chemicals by Paper Chromatography," J. Assoc. Off. Agr. Chem., 44(4):643+ (1961).

[2] Lukens, R. J., and H. D. Sisler, "2-Thiazolidinethione-4-Carboxylic Acid from the Reaction of Captan with Cysteine," Science, 127(3299): 650 (21 March 1958).

According to Lukens and Sisler (1958), the amino acid cysteine reacts with captan *in vitro* as follows:


[HO2CCH(NH2)CH2S-]
Cystine
Tetrahydrophthalimide
NSCCl3 + 2 HSCH2CH(NH2)CO2H
Captan
Cysteine
CO2H
2-Thiazolidinethione-4-carboxylic acid
CS2 + HCl + H2S

Captan itself appears capable of reacting only with thiol groups. However, initial reaction products containing the trichlorothio portion of the captan molecule and the thiophosgene released by interaction of captan with thiol groups are apparently capable of reacting with amino, hydroxyl, thiol, and possibly other groups. Chemical reactions of this kind within the cell are considered to be responsible for the fungitoxicity of captan.

Because captan reacts in a similar manner with sodium dimethyldithiocarbamate (Lukens, 1959)[1], it cannot be mixed with dithiocarbamate fungicides.

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[1] Lukens, R. J., "Chemical and Biological Studies on a Reaction Between Captan and the Dialkyldithiocarbamates," Phytopathology, 49(6):339-343 (June 1959).

Owens and Blaak (1960)[1] have further investigated the complex interactions of captan with thiols. Captan was shown to produce the corresponding disulfide when reacted with thiophenol or 4-nitrothiophenol. The work of Owens and Blaak (1960) confirmed the belief that thiophosgene is an intermediate in the reactions of captan with thiols.

Other Chemical Reactions - The basis for one analytical method for captan residues is fusion with resorcinol [$m\text{-}C_6H_4(OH)_2$] followed by a colorimetric determination. The structure of the product is still not known, but it is known to have the empirical formula $C_{13}H_8O_4S$ (Pomerantz, et al. 1969)[2].

Occurrence of Captan Residues in Food and Feed Commodities

The Food and Drug Administration (FDA), Department of Health, Education and Welfare, monitors pesticide residues in the nation's food supply through two programs. One program, commonly known as the "total diet program," involves the examination of food ready to be eaten. This investigation measures the amount of pesticide chemicals found in a high-consumption varied diet. The samples are collected in retail markets and prepared for consumption before analysis. The other program involves the examination of large numbers of samples, obtained when lots are shipped in interstate commerce, to determine compliance with tolerances. These analyses are complimented by observation and investigations in the growing areas to determine the actual practices being followed in the use of pesticide chemicals.

A majority of the samples collected in these programs are categorized as "objective" samples. Objective samples are those collected where there is no suspicion of excessive residues or misuse of the pesticide chemicals. All samples of imported foods and fish are categorized as "objective" samples even though there may be reason to believe excessive residues may be found on successive lots of these food categories.

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[1] Owens, G., and G. Blaak, "Chemistry of the Reactions of Dichlone and Captan with Thiols," Contrib. Boyce Thompson Inst., 20(8):475-497 (December 1960).

[2] Pomerantz, I., L. Miller, E. Lustig, D. Mastbrook, E. Hansen, R. Barron, N. Oates and J. Y. Chen, "The Fusion of Captan N-(Trichloromethylthio-4-Cyclohexene-1,2-Dicarboximide with Resorcinol," Tetrahedron Letters, (60):5307-5310 (December 1969).

Market-basket samples for the total diet studies are purchased from retail stores, bimonthly, in five regions of the United States. A shopping guide totaling 117 foods for all regions is used, but not all foods are represented in all regions because of differences in regional dietary patterns. The food items are separated into 12 classes of similar foods (e.g., dairy products; meat, fish and poultry; legume vegetables; and garden fruits) for more reliable analysis and to minimize the dilution factor. Each class in each sample is a "composite." The food items and the proportion of each used in the study were developed in cooperation with the Household Economics Research Division, USDA, and represents the high consumption level of a 16- to 19-year-old male. Each sample represents a 2-week supply of food.

Surveillance samples are generally collected at major harvesting and distribution centers throughout the United States and examined in 16 FDA district laboratories. Some samples may be collected in the fields immediately prior to harvest. Surveillance samples are not obtained in retail markets. Samples of imported food are collected when offered for entry into the United States.

DeBaun et al.[1/] investigated the nature of the residue on apple fruit and foliage under field conditions, using captan-^{14}C=O, but only partially characterized the residue. In surface washes of the fruit, the major component of the residue is captan (68-79%), lesser amounts of component THPI (5.2-7.6%), THPAM (tetrahydrophthalamic acid) (0.4-1.3%), and little or no captan-epoxide or THPI-epoxide ($<$ 1%). Captan-epoxide was not previously reported as a component of the residue. Upon analyzing the apple peel and pulp, it was found that captan predominated in the peel, while THPI predominated in the pulp, the remainder being THPAM, captan-epoxide and THPI-epoxide. The epoxides did not exceed 0.5 ppm in apple peel and 0.3 in apple pulp under the conditions of this investigation.

The data submitted to EPA by Chevron Chemical Company and Stauffer Chemical Company on feeding studies involving cattle and swine indicates only the carry-over of captan residues, THPI and THPAM[2-4/]. These studies were done before the metabolism was investigated by DeBaun, Hoffman and coworkers. Stauffer and Chevron Chemical Companies have conducted studies to investigate the metabolism more fully. However, in finding unexpected metabolites, they have reopened questions of whether or not the metabolites are toxic and whether or not they should be looked for as components of the residue. Tolerances regarding meat, milk, poultry and eggs are on an interim basis.

1/ Debaun, J. R., L. A. Gruwell, and J. J. Menn, "The Fate of Captan (carbony -^{14}C) on Field-Grown Apple Trees," Stauffer Chem. Co. report, May 1974.

2/ Harris Laboratories, "Captan Study," unpublished report to American Seed Trade Association, Lincoln, Nebr. (1972).

3/ Harris Laboratories, "Results from the Analysis of Hog Tissues for Tetrahydrophthalimide," unpublished report, Lincoln, Nebr. (February 1973).

4/ Industrial Bio-Test Laboratories, "Tissue Residue Study for Captan and Tetrahydrophthalimide in Crossbred Steers Fed Technical Captan," unpublished report to American Seed Trade Association, Northbrook, Ill. (December 1972).

Evaluation of the published data concerning pesticide residues in food has revealed that captan has not been reported as a significant residue in any food class. From conferences with FDA officials, it was learned that the analytical system used by the FDA laboratories (in Kansas City) does detect captan. However, the recoveries are low (about 50%) because analytical response is not good (detection of captan by the gas chromatographic procedure is somewhat erratic). However, captan residues are detected only occassionally in the total diet studies and analytical studies specifically for captan are not ordinarily performed.

Acceptable Daily Intake

The acceptable daily intake (ADI) is defined as the daily intake which, during an entire lifetime, appears to be without appreciable risk on the basis of all known facts at the time of evaluation (Lu, 1973)[1]. It is expressed in milligrams of the chemical per kilogram of body weight (mg/kg).

The ADI for captan is 0.125 mg/kg. This level was set at the 1965 Joint Meeting of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues. A major review was held again at the 1969 Joint Meeting (FAO/WHO, 1970), but any pesticide may be reviewed at any annual meeting if new evidence is available. The ADI for captan is considered a temporary value, but as of the 1971 Joint Meeting it has not been changed (FAO/WHO, 1972)[2]. All available research on captain's biochemical effects, toxicology, and teratology was used to determine the ADI.

Tolerances

U.S. Tolerances - Section 408 of the Food, Drug and Cosmetic Act, as amended, gives procedures for establishing tolerances for pesticide chemicals on raw agricultural commodities. Section 409 applies to food additives, including pesticide chemicals on processed foods. Tolerances for captan on raw agricultural commodities are published in the Code of Federal Regulations, Title 40. They are summarized in Table 2. Tolerances for processed foods are cited in Title 21 of the Code as: "50 ppm on captan residues in or on washed raisins when present as a result of fungicidal treatment by preharvest application to grapes and postharvest application during the drying process."[3]

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[1] Lu, F.C., "Toxicological Evaluation of Food Additives and Pesticide Residues and Their 'Acceptable Daily Intakes' for Man: The Role of WHO, in Conjunction with FAO," Residue Rev., 45:81-93 (1973).

[2] FAO/WHO, Food and Agricultural Organization of the United Nations/World Health Organization, "Pesticide Residues in Food," Report of the 1971 Joint FAO/WHO Meeting on Pesticide Residues, World Health Organization Tech. Rept. Series No. 502, Geneva (1972).

[3] Code of Federal Regulations, Title 21, Chapter 1, Subchapter B, Part 121, Subpart A, Section 123.40.

Table 2. U.S. TOLERANCES FOR CAPTAN ON RAW AGRICULTURAL COMMODITIES

ppm	Crop	ppm	Crop	ppm	Crop
2	Almonds	2	Collards	25	Pineapple
100	Almond hulls	2	Corn (sweet)	50	Plum (prunes)
25	Apples	2	Cottonseed	25	Potatoes
50	Apricots	25	Cranberries	25	Pumpkin
25	Avocados	25	Cucumbers	25	Quinces
25	Beans (dry or succulent)	25	Dewberries	25	Raspberries
100	Beet greens	25	Eggplant	25	Rhubarb
2	Beet roots	50	Grapes	2	Rutabaga
25	Blackberries	25	Honeydew melon	2	Soybeans (dry and succulent)
25	Blueberries (Huckleberries)	2	Kale	100	Spinach
		2	Kohlrabi	25	Strawberries
2	Broccoli	100	Lettuce	25	Squash (summer and winter)
2	Brussels sprouts	50	Mangoes	50	Tangelos
2	Cabbage	2	Mustard	25	Tomatoes
25	Cantaloupe	50	Nectarines	2	Turnips
2	Carrots	25	Onions, dry bulb		
2	Cauliflower	50	Onions, green		
50	Celery	50	Peaches		
100	Cherries	25	Pears		
25	Citrus (grapefruit, lemons, limes, oranges, tangerines)	2	Peas		
		25	Peppers		
		25	Pimento		

Source: U.S. Environmental Protection Agency, EPA Compendium of Registered Pesticides, Vol. II: Fungicides and Nematicides, Washington, D.C. (1973).

According to Lu (1973), U.S. tolerances which are established should not result in the maximum ADI being reached each day. He gives the following reasons:

1. The tolerance reflects the maximum level of residue resulting from good agricultural practice, but this level is often not reached.
2. The tolerance is based on the assumption that the particular pesticide is used on all food in the class in question, and this is rarely the case.
3. Much of the residue will be lost in storage, processing and cooking.

The tolerances are also based upon the entire product as purchased in the market. However, the product, as purchased, may not be entirely consumed.

International Tolerances - Tolerances established by individual nations may be based on recommendations of the FAO/WHO Expert Committee on Food Additives. The Committee evaluates all residue data submitted by interested parties and uses the following criteria (FAO/WHO, 1962)[1] for making tolerance recommendations:

1. Decide upon the effective level of the food additive under consideration that would be needed in good technological practice.
2. Examine the possible uses and list all the foods in which the food additive might be used.
3. Calculate the daily intake level that might occur if the food additive was used in all the foods for which it might be a useful additive, working on the basis of the average intake of the food materials containing the additive. This average intake for appropriate population groups is obtained from national food consumption surveys.
4. Obtain the necessary information from which to calculate the average body weight of the population group concerned (usually between 50 to 70 kg).
5. From this information, calculate the intake of the additive in milligrams per kilograms of body weight per day.

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[1] FAO/WHO, Food and Agricultural Organization of the United Nations/World Health Organization, "Evaluation of the Toxicity of a Number of Antimicrobials and Antioxidants," Sixth Report, Joint FAO/WHO Expert Committee on Food Additives, World Health Organization Tech. Rept. Series No. 228, Geneva (1962).

6. Check the figure against the acceptable intakes given for the substances in the table. If it falls within the unconditional intake zone, the situation is satisfactory and the level proposed may be accepted. If it falls within the conditional intake zone, further scientific advice is required before the level of use proposed is accepted.

The recommendations for captan tolerances established by the 1969 Joint Meeting of the FAO and WHO (FAO/WHO, 1972), are as follows:

Commodity	Tolerance (ppm)
Apples, cherries	40
Pear	30
Apricots	20
Citrus fruit, peaches, plums, rhubarb, tomatoes	15
Strawberries, raspberries, cranberries, cucumbers, lettuce, green beans, pepper	10
Raisins	5

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Pomerantz, I., L. Miller, E. Lustig, D. Mastbrook, E. Hansen, R. Barron, N. Oates and J. Y. Chen, "The Fusion of Captan N-(Trichloromethylthio-4-Cyclohexene-1,2-Dicarboximide with Resorcinol," *Tetrahedron Letters*, (60):5307-5310 (December 1969).

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART B. PHARMACOLOGY AND TOXICOLOGY

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This section is concerned with information on the acute, subacute and chronic toxicities of captan in laboratory and domestic animals (rats, mice, dogs, hamsters, rabbits, monkeys, chicken, swine, sheep, and cattle). A brief review is given of the characteristic symptoms and pathology of captan poisoning in mammals. The metabolism of captan is also discussed in relation to absorption, distribution, excretion, and biotransformation. Other subjects that have been reviewed are: the effects on reproduction, malformation of the young, and mutagenic effects. Limited investigations were found relating to the effects of captan on tissue culture. Data was also found on oncogenic effects and effects on man. The section summarizes rather than interprets data reviewed.

Acute, Subacute and Chronic Toxicity

Toxicity to Laboratory Animals -

Acute oral toxicity - rats - The acute oral toxicity of captan for rats ranges from 8,400 to 12,600 mg/kg body weight (see Table 3). The average LD_{50} from the data in the table is 10,000 mg/kg (FCH, 1970;[1] Ben-Dyke et al., 1970;[2] Krijnen and Boyd, 1970[3]).

There are no reported studies on differences in toxicity to captan among male and female rats. It appears reasonable to assume that males are as susceptible to oral dosing as females.

Krijnen and Boyd (1971)[4] performed a series of tests in which they showed that the LD_{50} of captan was influenced considerably by the nutritional state of the test animal (rat). They found that reduction of dietary protein to one-third of the optimal intake lowered the growth rate but did not have much effect on the oral LD_{50}. When rats were fed at protein levels which were one-seventh optimal intake (3.5% casein), they did not grow and were much more susceptible to captan intoxication. When rats were fed a diet containing no casein, they lost weight and were more susceptible to all pesticides tested; sensitivity to captan was increased 2,100 times. The LD_{50} was reduced from 12,600 mg/kg at optimal protein levels to 479 mg/kg at 3.5 casein.

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[1] Farm Chemicals Handbook, Meister Publishing Company, Willoughby, Ohio (1970).

[2] Ben-Dyke, R., D. M. Sanderson, and D. N. Noakes, "Acute Toxicity Data for Pesticides (1970)," World Rev. Pest. Cont., 9:119-127 (1970).

[3] Krijnen, C. G., and E. M. Boyd, "Susceptibility to Captan Pesticide of Albino Rats Fed from Weaning on Diets Containing Various Levels of Protein," Food Cosmet. Toxicol., 8:35-42 (1970)

[4] Krijnen, C. G., and E. M. Boyd, "The Influence of Diets Containing from 0 to 81 Percent of Protein on Tolerated Doses of Pesticides," Comp. Gen. Pharmacol., 2:373-376 (1971).

Table 3. THE TOXICITY OF CAPTAN - RATS

Sex and age of animals	Duration of test	Toxicity calculation	Toxicity measured	Comments on effect	References
Mixed sex, adults	--	LD_{50}, oral	9,000 mg/kg	--	a/
Mixed sex, adults	--	LD_{50}, oral	8,400 mg/kg	--	b/
Male, adults	28 days	LD_{50}, oral	12,600 mg/kg	--	c,d/
Male, adults	28 days	LD_{50}, oral	479 mg/kg	Diet was grossly deficient in protein	c,d,e/
Female, pregnant	3 days	Toxicity, dietary	2,000 mg/kg	Lowered weight gain of maternal animal only effect noted	f/
Mixed sex, adults	--	"No-effect level"	1,000 ppm diet = 50 mg/kg/day	--	g/
Male, young	100 days	LD_{50}, 100-day	916 mg/kg/day	--	h/

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a/ FCH, *op. cit.* (1970).

b/ Ben-Dyke et al., *op. cit.* (1970).

c/ Boyd, E. M., and C. G. Krijnen, "Toxicity of Captan and Protein-Deficient Diet," *J. Clin. Pharmacol.*, 8:225-234 (1968).

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f/ Kennedy, G., O. E. Fancher, and J. C. Calandra, "An Investigation of the Teratogenic Potential of Captan, Folpet, and Difolatan," *Toxicol. Appl. Pharmacol.*, 13:420-430 (1968).

g/ Anon., FAO/WHO, "Captan," *1969 Evaluations of Some Pesticide Residues in Food*, 33-44 (Geneva) (1970).

h/ Boyd, E. M., and E. Carsky, "The 100-Day LD_{50} Index of Captan," *Acta Pharmacol. Toxicol.*, 29:226-240 (1971).

In a study on teratogenic effects of captan, Kennedy et al. (1968) fed pregnant female rats for 3 days at 2,000 mg/kg and did not notice any toxic effects on the maternal animals except a lowered weight gain.

Subacute and chronic oral toxicity - rats - In a study of relatively long duration, Boyd and Carsky (1971) administered captan to young male rats by gavage in a range of doses once daily for 100 days (Table 3). The oral LD_{50} (100 days) was found to be 916 ± 233 mg/kg/day. In the survivors, the toxic syndrome subsided at 22 to 42 days and at this time the only symptoms which persisted were mild hypothermia and aciduria. From days 43 through 100 the captan-treated rats ate more food than the controls. At 100 days, however, the treated survivors weighed 30% less than the controls. At no time were there any significant changes in urinary blood, glucose or protein.

The 100 day LD_{50} index has been proposed as a single figure measurement of chronic lethal toxicity. The index is the LD_{50} (100 days) expressed as a percentage of the acute LD_{50} (one dose). Using the acute oral LD_{50} (one dose) of captan for rats (12.5 ± 3.5 g/kg) as reported by Boyd and Krijnen (1968) and the oral LD_{50} (100 days) found to be 0.916 ± 0.233 g/kg/day by Boyd and Carsky (1971), the oral 100 day LD_{50} index of captan was calculated to be 7.3 ± 1.9 (equivalent to 9,000 ppm) (Boyd and Carsky, 1971).

As reported by Boyd and Carsky (1971), inhibition of spermatogenesis was also particularly marked in rats which survived for 100 days (0.916 g/kg/day).

According to FAO/WHO (1970),[1] the upper level of captan which is toxicologically safe in rats is 1,000 ppm in the diet, equivalent to 50 mg/kg body weight per day.

In a study using mixed-sex adult rats, captan was fed for 13 weeks at several concentrations at a maximum level of 10,000 ppm. All experimental groups were started at a level of 500-ppm captan and the dosage was increased in gradual increments until a 5,000-ppm level was reached in 4 weeks and the 10,000-ppm level was reached after 7 weeks. The only effect noted was weight suppression with both males and females.[2]

A two-year study was conducted using both male and female rats. The test animals were fed diets that contained up to 5,000 ppm of technical captan. The female rats in the group which received 1,000 ppm of captan had a reduction in weight gain for the last 16 weeks of the test but were equal to controls for the first 88 weeks. Female rats receiving 5,000 ppm technical captan also displayed reduced weight gain.

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[1] FAO/WHO, "Captan," 1969 Evaluations of Some Pesticide Residues in Food, 33-34 (Geneva)(1970).

[2] Gray, E., Report of Hazelton Laboratories on Captan, EPA Pesticide Petition No. 15, 1954.

A second group of rats, both male and female, were given 10,000 ppm of technical captan for 24 weeks and then divided into two parts. One-half of the animals were then fed recrystallized captan for 30 weeks and one-half were continued on the technical material for 30 weeks. Both sexes on diets containing 10,000 ppm of either technical or recrystallized captan exhibited growth depression although signs of systemic toxicity were not observed. At autopsy indications of testicular atrophy were found in three animals.[1]

Acute toxicity - mice - The intraperitoneal LD_{50} was reported in a study by Arnold (FAO/WHO, 1970) to be 10 mg/kg body weight for the mouse (Table 4). Studies on acute oral toxicity, dermal toxicity, or inhalation toxicity were not found.

Subacute and chronic oral toxicity - mice - No subacute oral toxicity studies were found for mice. Only one reference to chronic studies with mice was found and this was the study of Innes et al. (1969), [2] which was conducted primarily as a study on the carcinogenic potential of captan (Table 4). In this test, male and female mice were given captan at a dose of 215 mg/kg body weight per day by gavage from 7 days of age to 4 weeks of age. From 4 weeks to 18 months, captan was added to the diet at 560 ppm. There was no indication that the fungicide caused an increased mortality.

Acute oral toxicity - dogs - Acute oral toxicity of captan for dogs was not reported in the literature examined in this study.

Subacute oral toxicity - dogs - No subacute oral toxicity studies were found for dogs. However, a well defined chronic study on captan toxicity was reported (Fogleman, 1955)[3]. Groups of four dogs were used, each consisting of two males and two females. The animals were started on a dose regime of 0 (Group I), 10 (Group II), 25 (Group III) and 50 (Group IV) mg/kg body weight of captan. At the beginning of week 10, the dose levels were increased from 25 to 50 mg/kg (Group III) and from 50 to 100 mg/kg (Group IV). At week 18, the doses were again increased to 100 mg/kg (Group III) and 300 mg/kg (Group IV). The captan was given to the dogs in gelatin capsules 6 days a week for 66 weeks.

All the dogs in Group I were normal at the completion of the test. Group II animals which had received 298 daily doses of captan (10 mg/kg/day) were normal and alert. They exhibited either maintenance or weight gains. The Group III dogs had received 54 daily doses of 25 mg/kg, 48 doses of 50 mg/kg, and then 100 mg/kg daily doses for the remainder of the test. These animals appeared normally alert and did not exhibit any signs of toxicity.

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[1] Weir, E., Report of Hazelton Laboratories on Captan, EPA Pesticide Petition No. 15, (1956).

[2] Innes, J. R. M., B. M. Ulland, M. G. Valerio, L. Petrucelli, L. Fishbein, E. R. Hart, A. J. Pallotta, R. R. Bates, H. L. Falk, J. J. Gart, M. Klein, I. Mitchell, and J. Peters, "Bioassay of Pesticides and Industrial Chemicals for Tumorigenicity in Mice: A Preliminary Note," J. Natl. Cancer Inst., 42(6):1101-1114 (1969).

[3] Fogleman, R., Report of Hazelton Laboratories on Captan, EPA Pesticide Petition No. 15 (1955).

Table 4. TOXICITY DATA ON CAPTAN - LABORATORY ANIMAL

Test animal	Condition and sex of animal	Duration of test	Toxicity calculation	Toxicity measured	Comments on effect	References
Mice	Mixed sex, adults	--	LD_{50}, i.p.	10 mg/kg	--	a/
Mice	Mixed sex, adults	18 months	Toxicity, dietary	560 ppm	Lethal toxic effects not noted	b/
Dogs	Mixed sex, adults	--	"No-effect level"	100 mg/kg/day	--	c/
Hamsters	Female, pregnant	15 days	Toxicity, dietary	1,000 mg/kg	Given from days 1-15 of gestation Lower gestational weight gain	d/
Hamsters	Female, pregnant	5 days	Toxicity, oral	500 mg/kg/day	20% mortality of mothers	e/
Rabbits	Female, pregnant	6 days	Toxicity, oral	80 mg/kg/day	Given during days 7-12 of gestation	f/
Rabbits	Female, pregnant	13 days	Toxicity, oral	75 mg/kg/day	Given on days 6-18 of gestation	d/
Rabbits	Mixed sex, adults	14 days	Toxicity, oral	500 mg/kg/day	Resulted in pathology being induced	g/
Monkeys	Female, pregnant	11 days	Toxicity, oral	25 mg/kg/day	Given on days 22-32 of gestation	h/
Monkeys	Female, pregnant	14 days	Toxicity, oral	75 mg/kg/day	Given on days 21-34 of gestation	i/
Monkeys	Mixed sex, adults	--	"No-effect level"	12.5 mg/kg/day	--	c/

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a/ Arnold (1967). Quoted in Anon., FAO/WHO report (1970).

b/ Innes et al., op. cit. (1969).

c/ Anon., FAO/WHO report, op. cit. (1970).

d/ Kennedy et al., op. cit. (1968).

e/ Robens, op. cit. (1970).

f/ Fabro, S., R. L. Smith, and R. T. Williams, "Embryotoxic Activity of Some Pesticides and Drugs Related to Phthalimide," Food Cosmet. Toxicol., 3: 587-590 (1965).

g/ Szuperski, T., and A. Grabarska, "Changes in Internal Organs of Rabbits after Experimental Oral Administration of Captan Fungicide," Zesz. Nauk. Szk. Roln. Olsztynie., 28:279-284 (1972).

h/ Courtney (1968). Quoted in Anon., FAO/WHO report (1970).

i/ Vondruska (1969). Quoted in Anon., FAO/WHO report (1971).

The animals in Group IV were also normally alert and, with the exception of one dog which had a weight loss, did not exhibit signs of toxicity. Liver and kidney weights were slightly increased in the dogs which received the 300-mg/kg dose. There was no evidence of systemic toxicity. Gross changes or histopathological changes in tissues due to treatment at any dose level were not observed. There were no significant changes in hematological or biochemical findings.

Acute oral toxicity - hamsters - An oral LD_{50} was not found in the literature for hamsters. Oral subacute toxicity was reported in a study by Robens (1970)[1] for pregnant females. The animals were fed captan for 5 days at 500 mg/kg body weight per day. The reported mortality following this dosage was 20%. Kennedy et al. (1968), in a study on the teratogenic effect of captan fed to pregnant female hamsters for 15 days at 1,000 mg/kg body weight, reported that lethal toxic effects were not observed although the females did exhibit a lowered gestational weight gain.

Chronic oral toxicity - hamsters - Data on the long-term effects of captan have not been reported for hamsters.

Acute oral toxicity - rabbits - Data on oral toxicity of captan to rabbits has not been determined by direct tests. Indirect toxicity data (mortality resulting during teratogenic tests, etc.) are all that are available in the open literature.

Subacute toxicity - rabbits - Fabro et al. (1965) gave pregnant New Zealand white rabbits daily oral doses of 80 mg/kg body weight of captan for 6 days (7 through 12 of gestation). These authors did not report any lethality. Lethal toxic effects were also not observed in a study by Kennedy et al. (1968) in which pregnant rabbits were treated for 10 days at a captan level of 75 mg/kg/day.

Oral subacute toxicity of captan administered at 500 mg/kg/day for 14 days (equivalent to 16,500 ppm) was studied by Szuperski and Grabarska (1973) in rabbits. These investigators reported that a dosage of 500 mg/kg/day level resulted in serious dystrophic changes in the kidneys, lungs, spleen, stomach, and intestinal mucosa. Captan at 500 mg/kg/day also inhibited the storage of polysaccharides, including glycogen, in the liver and muscles.

Chronic oral toxicity - rabbits - Reports on this subject with rabbits as the test animal were not found.

Acute oral toxicity - monkeys - Acute toxicity (LD_{50}) for captan in monkeys has not been reported. The only toxicity data that exist come from indirect tests where mortality or systemic toxic symptoms are reported in animals used primarily for teratogenic studies.

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[1] Robens, J. F., "Teratogenic Activity of Several Phthalimide Derivatives in the Golden Hamster," Toxicol. Appl. Pharmacol., 16:24-34 (1970).

Subacute toxicity - monkeys - According to Courtney, (FAO/WHO, 1970), lethal toxic effects were not observed in a test involving pregnant female monkeys fed captan at a level of 25 mg/kg/day for 11 days. Vondruska (FAO/WHO) reported the same findings for pregnant females fed 14 days at 75 mg/kg/day. FAO/WHO (1970) also reported that there were no adverse effects of 11-day captan dosages to monkeys at levels of 12.5 mg/kg/day.

Chronic oral toxicity - monkeys - Information on captan's chronic effects in monkeys has not been reported.

Potentiation - rats - The potentiation of toxicity of captan by DDT was considered in one study (Hazelton Laboratories, 1957).[1] Rats were treated by stomach tube with DDT, with captan, and with a combination of the two that contained 1 part DDT to 36 parts captan. Eight groups of four rats each were used in the test.

Potentiation was not observed. The acute toxicity (LD_{50}) of captan alone was determined to be 9,000 mg/kg.

Toxicity to Domestic Animals -

Acute oral toxicity - chickens - Acute LD_{50} values have not been reported for captan with chickens as the test animal.

Subacute and chronic oral toxicity - chickens - A feeding trial was conducted by Link et al. (1956)[2] in which chickens were fed under ordinary feeding conditions using corn that had been previously treated with captan. The test was started on 2-day-old chicks which were fed on a high energy ration containing corn that had been treated with 0.93 oz of captan per 100 lb (in the mixed ration, captan equaled 0.032%). The chicks were kept in electric brooders until 4 weeks of age at which time they were transferred to well-ventilated houses and fed from open feeders.

When mortality of the treated chicks was compared with that of the controls after 74 days of feeding, it was seen that captan in the ration had not resulted in increased mortality (see table 5).

Ackerson and Mussehl (FAO/WHO, 1970) were reported to have fed chicks a diet containing 320 ppm captan for 28 days without any observable detrimental effects.

The results of one study were reported in which groups of 15 hens were fed diets containing captan (technical) at 0, 100, 1,000, and 10,000 ppm for 90 days. The birds which received 100 and 1,000 ppm of the fungicide were reported normal in respect to food consumption, egg production, and survival. In those birds which were given diets containing 10,000 ppm

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1/ Hazelton Laboratories, Report on Captan, 1957, EPA Petition No. 124, amended.

2/ Link, R. P., J. C. Smith, and C. C. Morrill, "Toxicity Studies on Captan-Treated Corn in Pigs and Chickens," J. Am. Vet. Med. Assoc., 128:614-616 (1956).

Table 5. SUMMARY OF ORAL TOXICITY DATA FOR CAPTAN - DOMESTIC ANIMALS

Test animal	Sex and age of animal	Duration of test	Toxicity measured	Comments on effect	References
Chickens	Mixed sex, chicks	28 days	320 ppm	Lethal toxic effects not seen	a/
Chickens	Mixed sex, chicks	74 days	320 ppm	Lethal toxic effects not seen	b/
Swine	Mixed sex, adult	96 days	480 ppm	Remained normal	b/
Swine	Mixed sex, young	90 days	540 ppm	No abnormalities noted	c/
Swine	Mixed sex, weanlings	119 days	1,680 ppm	No gross pathological effects observed	d/
Swine	Mixed sex, adult	25 weeks	4,000 ppm	Toxicity not noted	e/
Cattle	Heifer	6 days	250 mg/kg/day	Lethal toxicity noted after 3 days	f/

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a/ Ackerson and Mussehl (1953). Quoted in Anon., FAO/WHO report (1970).

b/ Link et al., op. cit. (1956).

c/ Batte (1953). Quoted in Anon., FAO/WHO report (1970).

d/ Meade and Warner (1954). Quoted in Anon., FAO/WHO report (1970).

e/ Johnson, D. F., "A Toxicity Test of n-Trichloromethylthiotetrahydrophthalimide," Southwestern Vet., 8:55-57 (1954).

f/ Palmer, J. S., and R. D. Radeleff, "The Toxicologic Effects of Certain Fungicides and Herbicides on Sheep and Cattle," Ann. N. Y. Acad. Sci., 111:729-736 (1964).

captan, food refusal, weight loss and decreased egg production were observed. Autopsy did not reveal any gross pathological effects. By analysis it was also demonstrated that eggs and tissues of the hens did not store captan. Fertility and hatchability were not affected at any captan concentration tested.[1]

In a study of the teratogenic potential of captan, chickens were fed a diet containing 2,300 ppm technical captan (reported to be equal to 75 mg/kg body weight) for 6 weeks. Adverse effects were not observed on body weight gain, food consumption, behavior or egg production. Hatchability was not affected.[2]

Acute oral toxicity - swine - Reports dealing with the acute toxicity of captan to pigs were not found in the open literature of the sources used for this study.

Subacute and chronic oral toxicity - swine - Eight half-grown pigs (shoats) were fed captan-treated corn in a study conducted by Batte (FAO/WHO, 1970). Captan was incorporated in the diet to provide a level of 540 ppm. The feeding studies were carried out for three months. It was reported that the dietary administration of captan did not affect the rate of food consumption, the rate of growth or the general health of the animals when comparisons were made with control animals that had not received captan in their diet. It was also reported that there were no gross abnormalities observed in any of the animals on the captan diet.

According to Meade and Warner, weanling pigs have been fed diets containing captan at 420, 820, and 1,680 ppm for 119 days (FAO/WHO, 1970). It was reported that this study did not demonstrate any gross pathological lesions that could be attributed to the presence of captan in the diet.

It has also been reported that pigs fed 500 and 4,000 ppm captan in the diet did not develop any abnormal symptoms when fed the fungicide-treated ration for 22 to 25 weeks.

Link et al. (1956) conducted two feeding tests with pigs. In the first test seven gilts were used for trials and in the second, two gilts and two barrows were used. The test animals were fed a ration that consisted of corn treated with captan at 0.93 oz/100 lb. This ration was fed from self-feeders for 96 days.

The concentration of captan on the corn was calculated to be 0.058 and 0.048% in the finished feed.

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[1] Weir, R., Report of Hazelton Laboratories on Captan, 1957, EPA Pesticide Petition No. 15.

[2] Palazzolo, R., Report of Industrial Bio-Test Laboratories on Captan, 1966, EPA Pesticide Petition No. 15.

The presence of captan did not appear to affect the palatability of the ration so feed refusal was not a factor. Feed efficiency was slightly better in the treated animals than it was in the controls. Deaths were not observed in the treated group and histopathological examination of liver and kidney tissues failed to reveal any significant variations from normal. Chemical analysis of various tissues including fatty tissue also failed to reveal the presence of residues.

Differential leukocyte counts and total erythrocyte counts of captan-treated pigs differed little from similar counts on control animals indicating that the feeding of captan did not affect the blood-forming tissues.

Acute oral toxicity - sheep - **Acute toxicity data (LD_{50}) were not available in the non-proprietary literature used for this study. However, Palmer (1963)[1] conducted one test to determine acute toxicity of captan to sheep after a single oral dose.**

Wethers at least 1 year old were used in these tests and were treated with captan administered with a dosing syringe. Four sheep were used; one for each of two dose levels and two for one dose. Observations were carried out for 5 weeks after dosing.

The results of these acute tests are as follows:

Dose (mg/kg)	Observed effect	Results of observed effect
200	None	None
250	Poisoned	Died
250	Poisoned	Recovered
500	Poisoned	Died

The sheep treated at the highest level (500 mg/kg) showed evidence of cardiac deficiency with excessive fluid in the thoracic and abdominal cavities. The liver exhibited petechial hemorrhages, the gall bladder was distended and the gastrointestinal tract was acutely inflamed.

Data presented by Palmer and Radeleff (1964) show that sheep are regularly poisoned by single doses of 250 mg/kg or higher but that at levels of 50 to 100 mg/kg the animals can eliminate most of the material without showing any signs of toxicity.

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[1] Palmer, J. S., "Tolerance of Sheep to Captan," J. Am. Vet. Med. Assoc., 143:513-514 (1963).

Subacute and chronic oral toxicity - sheep - Sheep given captan at levels of 100 and 200 mg/kg body weight 5 days a week for 23 weeks developed depression and anorexia with weight loss. After captan administration was discontinued the animals recovered without complications.

Sheep which were given captan 5 days per week for 23 weeks at 5 to 50 mg/kg body weight did not evidence any ill effects when compared with the untreated controls (Palmer, 1963).

Acute oral toxicity - cattle - Toxicity data for captan to cattle are very limited and acute LD_{50} values do not exist.

Subacute toxicity - cattle - One study was reported in which one animal was given multiple doses of captan at 250 mg/kg for six doses. It was reported that the animal died and that symptoms of poisoning were present after the first three doses (Palmer and Radeleff, 1964). Symptoms of poisoning were reported as diarrhea and abortion.

Dermal Effects

Studies of captan's irritation potential on rabbits demonstrated that the compound had very low irritation and little or no sensitizing properties for the rabbit. In studies with guinea pigs, when ten daily intracutaneous injections of 0.1 ml of 0.1% captan in normal saline served as the sensitizing dose, the challenge or elicitation tests demonstrated captan to be a moderate sensitizer. In human patch tests, a captan paste (50% captan in water) when applied directly to the skin caused no irritation after 24 hr of continuous application (R.T. Vanderbilt Co., Inc., 1969)[1].

Symptomatology and Pathology Associated with Mammals

Symptomatology - The signs of intoxication most often reported for sheep have been depression and anorexia with weight loss, the degree depending upon the dosage. After captan is discontinued symptoms disappear without complication.

The clinical signs of intoxication of rats with captan, as reported by Boyd and Kirjnen (1968), include: irritability, epistaxis, listlessness, soft stools, soiling of fur, hypothermia, anorexia, oligodipsia, loss of body weight, oliguria, alkalinuria, glycosuria, and hematuria.

Irritability, epistaxis, listlessness and soft stools reached a peak of intensity on the second and third days.

The listlessness observed was considered to be due in part to a fall in body temperature which reached a maximum at 24 hr (dose dependent). On the third and fourth days, diuresis and aciduria occurred. The immediate cause of death was cardiac or respiratory failure.

1/ R. T. Vanderbilt Co., Inc. Vancide® 89: Summary Report of Toxicity Tests, Technical Data Sheet (April 23, 1969).

Table 6. HISTOPATHOLOGICAL OBSERVATIONS ON RATS ADMINISTERED CAPTAN

Organ	At death within 48 hours	At death during first 24 days	In survivors at 100 days
Adrenal glands	Normal appearance	Lipoid droplets prominent in cortex	Lipoid droplets prominent
Brain	Hemorrhagic capillary-venous congestion of brain and meninges	Areas of capillary-venous congestion of cerebrum, cerebellum and meninges	Mild hypernemia
Gastrointestinal tract			
cardiac stomach	Marked capillary-venous congestion of the lamina propria and submucosa, hemorrhagic, leukocyte-infiltrated ulcers	Congestion of the lamina propria with infiltrative ulcers	Hypertrophy of the stratified squamous epithelium
pyloric stomach	Marked vascular congestion at the mouths of the gastric glands	Congestion with hemorrhagic necrotic ulcers	Normal appearance
small bowel	Capillary-venous congestion of the villi	Congestion of the villi and submucosa	Hypertrophy and hypernemia
cecum	Marked capillary-venous congestion and hemorrhage of the lamina propria and submucosa	Capillary-venous congestion of the lamina propria and submucosa	Hypertrophy and hypernemia
colon	Vascular congestion of the lamina propria and submucosa	Mild congestion	Normal appearance
Heart	Occasional capillary congestion and hemorrhage	Normal appearance	Normal appearance
Kidneys	Marked capillary-venous congestion, especially in the loop region	Capillary-venous congestion in the region of the loop of Henie, occasional tubular cloudy swelling and infection	Mild cloudy swelling of the tubules
Liver	Sinusoidal congestion; cloudy swelling of the hepatic cells	Diffuse cloudy swelling	Normal appearance
Lungs	Normal appearance; some hypernemia or congestion	Oedema, congestion, venous thrombosis and occasionally pneumonitis	Areas of capillary-venous congestion
Muscle (ventral abdominal wall)	Cross striation weak	Normal appearance	Normal appearance
Pancreas	Capillary-venous congestion	--	--
Salivary (submaxillary) glands	Normal appearance	Deficiency of serous zymogenic granules	Minor deficiency of zymogenic granules
Skin	Normal appearance	Normal appearance	Normal appearance
Spleen	Normal appearance	Red pulp atrophied imbeculae prominent	Normal appearance
Testes	Vascular congestion of interstitial tissue	Marked inhibition of spermatogenesis, interstitial congestion	Deficiency of normal sperm
Thymus gland	Capillary-venous congestion and mild loss of thymocytes	Marked loss of thymocytes, atrophy	Marked loss of thymocytes, atrophy

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Data from Boyd and Krijnen (1968) and Boyd and Carsky (1971).

Recovery of survivors was accompanied by diuresis and a rapid gain in body weight. After 4 weeks, the weight, water content and appearance of body organs were practically normal.

Pathology - Gross pathology has been described in detail only for the rat, but the clinical signs should be similar for most mammals.

The gross pathology observed at autopsy on rats which died of captan intoxication was reported by Boyd and Krijnen (1968). The lesions and percent incidence observed were splenic atrophy (87%), congested brain and meninges (67%), atrophy of thymus gland (60%), dark liver (60%), gastric ulcers (33%), hemorrhagic small bowel (16%), congested stomach (13%), erect, edematous penis (10%), congested cecum and colon (6%), and congested lung (6%).

It can be seen that splenic atrophy is observed regularly and that the majority of dead animals also exhibit congested brain and meninges, atrophied thymus gland and a dark liver (Boyd and Krijnen, 1968).

A summary of histopathological observations, when death occurs early (48 hr), late (21 days), and in survivors is presented in Table 6. This table is a combination of the results presented by Boyd and Krijnen (1968) and Boyd and Carsky (1971).

Summary - The level of captan causing no significant toxicological effects in monkeys and dogs was 12.5 mg/kg/day and 100 mg/kg/day, respectively.

The LD_{50} in rats ranges from approximately 8,400 to 12,600 mg/kg of body weight.

Swine have consumed 4,000 ppm of captan over a 175-day period without the appearance of any toxic symptoms.

Based on one investigation, cattle seem to be more sensitive to captan than some other species, six doses of 250 mg/kg/day produced lethality. Also, another ruminant species, sheep, is poisoned by single doses of 250 mg/kg or higher.

The symptoms of captan poisoning in rats are irritability, epistaxis, listlessness, hypothermia, anorexia, oligodipsia, loss of body weight, oliguria, alkalinuria, glycosuria and hematuria.

The LD_{50} in rats ranges from approximately 8,400 to 12,600 mg/kg of body weight.

Metabolism of Captan

Absorption - Engst and Raab (1973)[1] reported that captan is rapidly absorbed from the rat gastrointestinal tract.

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[1] Engst, R., and M. Raab, "Zum Metabolismus fungizider Phthalimid-Derivate in lebens - mittelchemischtoxikologischer Sicht," Nahrung, 17:731-738 (1973).

Distribution - Captan is rapidly decomposed in both human and rabbit blood in vitro experiments. When 500 mg/kg captan was injected into rabbits, no captan could be detected in the blood during a 56-hour sampling period. The metabolite tetrahydrophthalalimide (THPI) reached a peak concentration of 25 µg/ml at 25 hours (Crossley, 1967).[1] Feeding studies with captan demonstrated that it was not stored in eggs or flesh of poultry or the tissues of pigs (Anon., FAO/WHO report, 1970).

Excretion - Engst and Raab (1973) reported that a given dose of captan was virtually completely excreted in the feces of rats within 3 days. It has been suggested (Anon., FAO/WHO report, 1970) that tetrahydrophthalamic acid is a principal metabolite of captan excreted in the urine.

The metabolic fate of captan in albino rats was reported by DeBaun et al. (1974).[2] These investigators conducted their studies using a trichloromethyl-^{14}C-captan and determined the distribution of orally administered captan 4 days after treatment. They found that 51.8% was present in urine, 22.8% in expired air, 15.9% in feces and 0.6% in tissues.

The ^{14}C activity associated with the tissues after oral treatment with [^{14}C] captan was reported to probably be due to incorporation of $^{14}CO_2$ into tissue macromolecules via intermediary metabolic routes.

Metabolism of captan may involve the evolution of thiophosgene which is detoxified in part by at least three mechanisms: (1) oxidation and/or hydrolysis to CO2; (2) reaction with a cysteine moiety to yield thiozolidine-2-thione-4-carboxylic acid; and (3) reaction with sulphite to produce dithiobis (methanesulphonic acid). The gastrointestinal tract probably plays a major role in degradation of captan and its metabolism.

Large accumulations of captan in general and in specific organs in particular were not observed. There were no significant differences between tissue residue values obtained from male or female animals.

Biotransformation - Shtenberg (1972)[3] reported that the toxicity of captan was 26 times greater in animals kept on a protein deficient diet. Nelson (1971)[4] found that captan induces mitochondrial swelling in rat liver. In the absence of an energy source, initial swelling can be inhibited by 2,4-dinitrophenol and KCN. These two chemicals do not inhibit later swelling, indicating a two-phase phenomenon--one energy-dependent and the other a passive phase. The trichloromethyl moiety of captan was found to be the active portion that induced mitochondrial swelling. It was assumed that captan interacts with mitochondrial membranes, presumably sulfhydryl groups. According to Engst and Raab (1973), 5% of an LD_{50} dose of captan given to rats produces a 54% reduction of erythrocyte SH levels within 3 hr. The reduction of SH groups was still 25% after 24 hr. Serum and liver SH groups were also diminished by 18% and 11%, respectively. Serum glutamic-pyruvic transaminase and lactic dehydrogenase activities were reduced about 20%. No captan could be detected in the blood by gas chromatographic or thin-layer chromatographic techniques. Only metabolites tetrahydrophthalimide and tetrahydrophthalic acid could be detected.

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[1] Crossley, J., "The Stability of Captan in Blood," Unpublished report, file no. 721.11, Chevron Chemical Co., Richmond, Calif. (October 2, 1967).

[2] DeBaun, J. R., J. B. Miaullis, J. Knarr, A. Mihailovski, and J. J. Menn, "The Fate of N-Trichloro[^{14}C]methylthio-4-cyclohexene-1,2-dicarboximide ([^{14}C]captan) in the Rat," Xenobiotica, 4:101-119 (1974).

[3] Shtenberg, A. E., "Diet Background and the Body Sensitivity to Toxic Substances," Gig. Sanit, 37:73-76 (1972).

[4] Nelson, B. D., "Induction of Mitochondrial Swelling by the Fungicide Captan," Biochem. Pharmacol., 20(4):749-758 (1971).

Recent investigations by DeBaun, Hoffman and coworkers have further clarified the nature of the residue by feeding radio-labeled captan to the rat. Of special interest here is the work of Hoffman et al. (1973)1/ who identified a number of unexpected, previously unreported metabolites from the 1,2-dicarboximido-4-cylohexene (tetrahydrophthalimide or THPI) moiety of captan. These metabolites arose in three of four pathways after the hydrolytic cleavage of captan-^{14}C=0 to THPI and trichloromethylthio moieties. The major pathway in the rat apparently involves ring hydroxylation of the THPI to 3-OH-THPI, and further degradation to 3-OH-THPAM. The second pathway involves epoxidation of THPI to THPI-epoxide, followed by hydrolysis to 4,5-di-OH-THPI. (See Figure 4.) If the urinary distribution is any indication, then it would appear that the major component of the residue is 3-OH-THPI (38%), lesser amounts of component THPI (15%), other metabolites including THPI-epoxide (5-12%), and little if any captan *per se* (0.4%).

Gale et al. (1971)2/ demonstrated that *in vitro* captan was a potent inhibitor of incorporation of thymidine, purine, and L-leucine into the acid insoluble fraction of Ehrlich ascites tumor cells. Prior addition of sulfhydryl groups or albumin to the media prevented this effect. Glycolysis was highly sensitive to captan; this could be prevented with added thiol groups also.

1/ Hoffman, L.J., J. R. Debaun, J. Knarr, and J. J. Menn, "Metabolism of N-(trichloromethylthio)1, 2-dicarboximido ^{14}C-4-cyclohexene (Captan) in the Rat," Stauffer Chemical Co., Westport, Conn. (August 1973).

2/ Gale, G.R., A. B. Smith, L. M. Atkins, E. M. Walkers, Jr., and R. H. Gadsden, "Pharmacology of Captan: Biochemical Effects with Special Reference to Macromolecular Synthesis," *Toxicol. Appl. Pharmacol.*, 18:426-441 (1971).

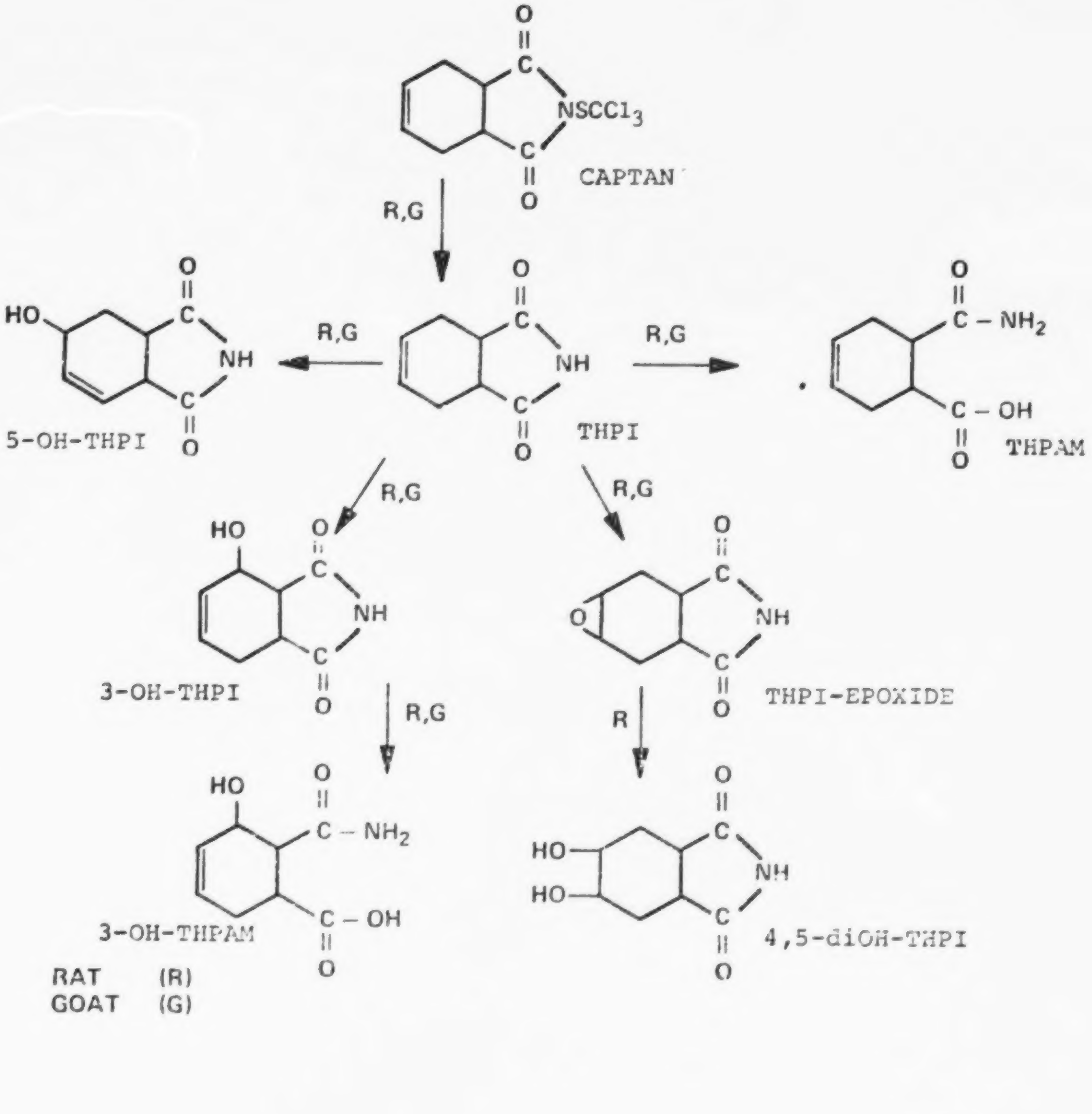
CAPTAN
NSCCl3
R,G
THPI
5-OH-THPI
THPAM
C – NH2
C – OH
3-OH-THPI
THPI-EPOXIDE
R
3-OH-THPAM
4,5-diOH-THPI
HO
NH
RAT (R)
GOAT (G)

Figure 4. Metabolic Pathway for Captan-^{14}C=O in the Rat and Goat

A report by the World Health Organization (FAO/WHO, 1970) suggests that in the presence of cysteine or glutathione, captan is matabolized to tetrahydrophthalimide, thiophosgene and chloride ion, carbon disulfide and sulfide. If cysteine is present, an additional compound, a substituted thiazolidinethione, has also been identified. Menzie (1969)[1] points out that the carbon disulfide was erroneously identified and should really be carbonyl sulfide, as identified by gas chromatography.

Summary -

1. Captan is rapidly absorbed from the gastrointestinal tract and rapidly destroyed in the blood.

2. It does not accumulate in the tissues of pigs or chickens.

3. Captan reacts readily with cysteine, glutathione, or other compounds containing SH groups.

4. Captan induces mitochondrial swelling by two mechanisms, one of which is energy dependent.

5. The major metabolic products of captan are tetrahydrophthalimide, chloride ion, thiophosgene, carbonyl sulfide, hydrogen sulfide, and 2-thiazolidinethione-4-carboxylic acid.

Effects on Reproduction

Laboratory Animals - A three-generation reproductive study (FAO/WHO, 1970) was conducted with rats which received technical captan in their diet in concentrations of 0, 100, 500,and 1,000 ppm. Groups of 16 female animals were used and two litters were produced in each generation. No significant differences were found between control and captan-treated rats with respect to fertility, gestation, viability or lactation indices or in the weanling weights in the first two generations. No effects were observed in the third generation except a slightly lowered lactation index for the group receiving 1,000 ppm of captan. Histopathological examination of tissues from 10 pups receiving 1,000 ppm captan in the third generation revealed no damage.

A study by Zhorzholiani (1971)[2] indicated that captan is gonadotropic. Rats and mice given daily oral doses of captan at 6 to 57 mg/kg and 2.5 to 20 mg/kg body weight, respectively, showed decreased sperm motility and abnormal changes in fetal development.

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[1] Menzie, C. M. "Captan," Metabolism of Pesticides, U.S. Bureau of Sport Fisheries and Wildlife, Special Scientific Report--Wildlife No. 127, 67-71 (1969).

[2] Zhorzholiani, V. S., "Effect of Prolonged Administration of Captan on the Function of the Gonads," Soobshch. Akad. Nauk. Gruz., SSR, 64(3):749-751 (1971).

Studies on the effect of captan on the reproductive fitness of DBA/2J male mice were performed by Collins (1972b).[1] Polygenic reproductive fitness was tested using two generations of male mice given oral doses of 50 to 100 mg/kg body weight per day for 5 days. A known mutagen, triethylenemelamine (TEM), was used as the positive control. TEM produced decreases in overall productivity (as measured by the fertility index) and decreased survival from birth to day 4, and from day 5 to weaning at 21 days. Captan-treated animals showed a decrease in fertility index, although neither dose rate produced as severe decreases as TEM administered at the rate of 0.1 mg/kg body weight. A decrease in average weaning weight was also observed in the first litter of the second generation for the 100 mg/kg dosage of captan.

Domestic Avian Species - Technical grade captan was fed to hens at levels of 100, 1,000 and 10,000 ppm for a period of 90 days:

Group No.	Hens	Roosters	Captan (ppm)
1	15	3	0
2	15	--	100
3	15	--	1,000
4	15	3	10,000

Captan did not alter fertility or hatchability at any level. There was a reduction in food consumption of the birds on the 10,000-ppm diet which caused a decrease in weight. The number of eggs produced by this group was reduced by 80% compared to the controls. No gross pathology was observed (Weir, 1957).

Hens in one study consumed a diet containing 2,300 ppm (equivalent to 75 mg/kg body weight) captan. The test group (five male and 18 female leghorn chickens) was maintained on the diet for 6 weeks. One female in the test group died, none in the controls. The control hens produced 432 eggs; the treated hens produced 428 eggs. Slightly more than 70% of the control eggs hatched and 77.1% of the test eggs hatched. No abnormal physical or behavioral reactions were noted in either test or control groups[2].

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[1] Collins, T. F. X., "Effect of Captan and Triethylenemelamine (TEM) on Reproductive Fitness of DBA/2J Mice," Toxicol. Appl. Pharmacol., 23:277-287 (1972b).

[2] Palazzolo, R., Industrial Bio-Test Laboratories Report on Captan, EPA Pesticide Petition No. 124.

Teratogenic Effects

Teratology is the study of congenital malformations. The teratogenicity of a compound is the result of damage to certain cells, or their death in a developing organism at some point where the susceptibility is at a maximum. Avian teratology involves damage to the embryo that may bring about death or cause malformations (Durham and Williams, 1972)1/.

The structure of captan has a moiety (ortho dicarboximido) similar to that of the proven teratogen, thalidomide. This similarity has prompted studies on the teratogenic effects of these compounds to laboratory animals. From a metabolic point of view, the breakdown of captan is not like that of thalidomide; captan has an easily broken N-S bond, thalidomide has a strong N-C bond.

In 1970, a search was made for metabolites of thalidomide which might be similar to those found in the degradation products of captan, folpet and captofol. No chemical compounds were found in common. The formation of an aliphatic fragment due to hydroxylation, decarboxylation, and/or other reactions from phthalic and tetahydrophthalic moieties is conceivable, but whether this aliphatic fragment would be associated with teratogensis is doubtful because of its instability and lack of known toxicity.

Investigations of biological effects, enzyme inhibition, and teratogenesis have revealed that it is the intact molecule (thalidomide) which causes malformations. However, since the intact thalidomide molecule has been shown to have teratogenic activity, and since the breakdown of captan differs from thalidomide, the concern for the possible teratogenic effect of captan as it related to thalidomide is not supported.

Monkeys - In a study by Courtney (FAO/WHO, 1968) groups of seven pregnant rhesus monkeys were given daily oral doses of 6.25, 12.5 or 25 mg/kg body weight of captan on days 22 through 32 of gestation. Thalidomide was used as a positive control at dosage levels of 5 mg/kg body weight per day in six animals and at 10 mg/kg body weight per day in four animals. Fetuses were recovered on approximately day 84 of gestation by caesarian section. The fetuses were examined for organ and skeletal defects. Fetal mortality occurred in three of seven monkeys at the 25 mg/kg level. The fetal mortality in the parent colony not fed captan was 13.2% on 439 conceptions. There was no abnormality among any fetuses in either of the three dose levels of captan.

1/ Durham, W. F., and C. H. Williams, "Mutagenic, Teratogenic, and Carcinogenic Properties of Pesticides," Ann. Rev. Entomol., 17:123-148 (1972).

In another study (Vondruska et al., 1971)[1] captan was administered orally to a group of pregnant monkeys (Rhesus and stump tail) at levels of 10, 25, and 75 mg/kg body weight. Doses were given on days 21 through 34 of gestation. Thalidomide was also administered to a positive control group at levels of 5 and 10 mg/kg body weight. As shown in Table 7, neither abnormal fetuses nor abortions occurred in the captan-fed group. No systemic toxic effects were observed in the mothers, even though exposure was for longer periods of time and at higher levels than with thalidomide.

Rabbits - During a study by Fabro (1965) four pregnant New Zealand white rabbits were given daily oral doses of 80 mg/kg body weight during days 7 to 12 of gestation. Five additional rabbits were given oral doses of 150 mg/kg body weight of thalidomide (positive controls) and five rabbits, used as negative controls, received no treatment. As indicated in Table 8, no embryotoxicity was observed in litters from the captan-fed rabbits.

In a more detailed study by Kennedy et al. (1968) a group of six pregnant Dutch belted rabbits were given 75 mg/kg body weight per day of technical captan, orally on days 6 through 16 of gestation. Three other groups, each containing five to seven New Zealand white rabbits, were given 18.75, 37.5 or 75 mg/kg body weight per day on days 6 through 18 of gestation. A control group (no treatment) and a positive control group (75 mg/kg thalidomide) were included. Two additional groups of Dutch belted rabbits were given oral doses of 75 mg/kg body weight of the captan metabolites phthalimide and tetrahydrophthalimide (THPI). As shown in Table 8, no teratogenic effects were observed with captan or the two metabolites. Young obtained from treated does appeared grossly normal, possessed well-defined skeletal structures, were of normal size and showed excellent survival during a 24-hr incubation period following recovery at gestation day 29. Females given thalidomide

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[1] Vondruska, J. F., O. E. Faucher, and J. C. Calandra, "An Investigation into the Teratogenic Potential of Captan, Folpet, and Difolatan in Nonhuman Primates," Toxicol. Appl. Pharmacol., 18:619-624 (1971).

Table 7. RESULTS OF CAPTAN AND THALIDOMIDE ADMINISTRATION TO PREGNANT MONKEYS

Test material	Dose (mg/kg)	Gestational days of dosing	Pregnant females dosed	Normal fetuses	Abnormal fetuses	Abortions
Captan	10.0	21-24	3R,4S	3R,4S	--	--
	25.0	21-34	7R	7R	--	--
	75.0	21-34	3R,4S	3R,4S	--	--
Thalidomide	5.0	26-28	2S	--	2S	--
	5.0	24-30	1S	--	1S	--
	10.0	25-27	11R,3S	2R	6R,2S	3R,1S
	10.0	24-30	1S	--	--	1S
	10.0	23-29	2S	--	--	2S

R = Rhesus monkeys; S = stump-tailed macaques.
Data from Vondruska et al., op. cit. (1971).

Table 8. TERATOGENIC ACTIVITY OF THALIDOMIDE, CAPTAN AND CAPTAN METABOLITES IN RABBITS

Species	Compound	Oral dose (mg/kg)	Number of pregnant females	Dosed, gestational days	Total number of implantations	Average number of implantations	Number of resorptions	Average litter size	Number of normal fetuses	Number of terata	Reference
Rabbit	None	--	5	--	41	8.2	3	7.6	38	0	
Rabbit	Thalidomide	150*	5	7-12	46	9.2	19	5.4	18	9	a/
Rabbit	Captan	80	4	7-12	37	9.2	3	8.5	34	0	
Rabbit DB†	None	--	7	6-16	52	7.4	0	7.4	51	1	
Rabbit NZ‡	None	--	10	6-18	66	6.6	2	6.4	64	0	
Rabbit DB	Thalidomide	75.0*	7	6-16	55	7.9	15	5.7	26	14	b/
Rabbit NZ	Thalidomide	75.0	10	6-18	74	7.4	10	6.4	40	24	
Rabbit DB	Captan	75.0	6	6-16	43	7.2	1	7.0	42	0	
Rabbit NZ	Captan	18.75	6	6-18	46	7.7	11	5.8	35	0	
Rabbit NZ	Captan	37.5	7	6-18	56	8.0	2	7.7	54	0	
Rabbit NZ	Captan	75.0	5	6-18	39	7.8	33	1.2	6	0	
Rabbit DB	Phthalimide**	75.0	10	6-16	66	6.6	3	6.3	63	0	
Rabbit DB	THPI**	75.0	9	6-16	66	7.3	9	6.3	57	0	

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* Daily oral dose.

† Dutch belted (thalidomide susceptible).

‡ New Zealand white (thalidomide susceptible).

** Captan metabolite.

a/ Fabro et al., op. cit. (1965).

b/ Kennedy et al., op. cit. (1968).

at the same dose level produced young which exhibited mild to severe limb abnormalities, attesting to the sensitivity of the two rabbit strains employed.

The only work reported for rabbits in which malformed fetuses were observed is that of McLaughlin et al. (1969).[1] In this study, groups of nine pregnant New Zealand white rabbits were given captan at dose levels of 37.5, 75 or 150 mg/kg body weight per day from days 6 through 16 of gestation. Thalidomide, used at the rates of 75 and 150 mg/kg body weight, produced the usual teratogenic response. Captan at 75 mg/kg body weight of the mother caused nine malformed individuals from 75 implantation sites of six does. Among the malformations were deformed limbs, cleft lip, and fused upper lip at the 75 mg/kg dosage. At the 37.5-mg/kg dosage the one malformed individual was acephalic.

Dogs - Earl et al. (1974)[2] conducted a study of the effects of captan on reproduction and the young of dogs. They fed three groups of dogs (five per group), 15, 30 and 60 mg/kg/day of captan, respectively, throughout the gestation period. They had a dog colony, not used in this study, which consisted of 48 females. These dogs had the following reproductive record. The percent that became pregnant was 87.5% (42 out of 48 females). The average litter size was 4.8 pups. Two percent were born dead. There were 5.1% resorptions. The following abnormalities occurred in 203 pups: nine subcutaneous hemorrhages, one abdominal hemorrhage, two cerebral edemas, two congestive kidneys, one subcutaneous edema, two front leg terata, one cleft palate, and one short tail.

The control dogs in this particular study produced 6.6 pups per litter and 10% were stillborn. Of the five dogs that received 15 mg/kg/day, only two became pregnant and of the pups produced 18.2% were stillborn. One pup had a single kidney. It was the investigator's experience that single kidney occurred once out of 500 births in control dogs. All five dogs became pregnant on the 30-mg/kg/day level. The average litter size was 6.8 pups. There were 20.6% stillborn. Three of the pups born alive had abnormalities. Two pups had crooked tails and one had gastroschisis. Five of the dozen bitches given the 60-mg/kg/day level of captan had pups.

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[1] McLaughlin, J. P., E. F. Reynaldo, J. K. Lamar, and J. P. Marlaio, "Teratology Studies in Rabbits with Captan, Folpet and Thalidomide," *Toxicol. Appl. Pharmacol.*, 14:641 (1969).

[2] Earl, F. L., E. Miller, and E. J. van Loon, "Reproductive Teratogenic and Neonatal Effects of Some Pesticides and Related Compounds in Beagle Dogs and Miniature Swine," E. D. William and B. Deichmann, *Pesticides and the Environment, a Continuing Controversy*, Intercontinental Medical Book Corporation, New York, New York (1974).

The average litter size was 4.4 pups. Only one pup was stillborn. One pup had a dome-shaped skull and was hydrocephalic. One pup had an open fontanelle; another pup had a single kidney.

When captan was administered in the diet of beagles at doses of 0, 30, or 60 mg/kg/day, either throughout gestation or throughout gestation with an eight week lactation period, no signs of teratogenecity or embryotoxicity were noted. Survival of the pups during the lactation period was not affected by captan (Kennedy et al.)[1].

Hamsters - In a study performed by Kennedy et al. (1968), groups of pregnant female hamsters were fed diets containing sufficient concentrations of captan so that the animals received an average daily intake of 0, 125, 250, 500 and 1,000 mg/kg body weight from days 1 through 15 of gestation. At day 15, all females were sacrificed, the young were surgically removed and the fetal development and structural formation of each were examined. As indicated in Table 9, the incidence of abnormal effects was not greater in any test group than in the controls. A significant increase in fetal resorption was observed at the dose level of 1,000 mg/kg body weight. The following terata were observed in hamster fetuses by Kennedy et al. (1968):

Dose level (mg/kg)	Finding	Incidence %
125	Total abnormal	3.1
	Meningoencephalocele	0.6
	Microphthalmia	2.5
250	Total abnormal	1.8
	Microphthalmia	0.9
	Developmental retardation	0.9
500	Total abnormal	3.5
	Cranial blister	1.2
	Exencephaly	0.6
	Shortened forelimb	0.6
	Gross developmental retardation	1.2
1,000	Total abnormal	3.1
	Microphthalmia	3.1
Control	Total abnormal	5.8
	Microphthalmia	1.6
	Caudal vertebrae absent	0.5
	Absence of eye pigmentation	2.6
	Facial hematoma	0.5
	No skeletal structures present	0.5

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[1] Kennedy, G., O. E. Fancher, and J. C. Calandra, "Tetratologic Evaluation of Captan in the Beagle Dog." unpublished report, Industrial Bio-Test Laboratories, Inc., Northbrook, Illinois (undated).

Table 9. TERATOGENIC ACTIVITY OF CAPTAN IN HAMSTERS

Species	Compound	Oral dose (mg/kg)	Number of pregnant females	Dosed, gestational days	Total number of implantations	Average number of implantations	Number of resorptions	Average litter size	Number of normal fetuses	Number of terata	References
Golden hamster	Corn oil (control)	--	21	--	212	10.1	23	9.0	180	11	a/
Golden hamster	Captan	125*	19	1-15	194	10.2	33	8.5	161	5	
Golden hamster	Captan	250	15	1-15	149	9.9	33	7.7	115	2	
Golden hamster	Captan	500	23	1-15	213	9.3	40	7.5	167	6	
Golden hamster	Captan	1,000	14	1-15	108	7.7	76	2.3	32	1	
Golden hamster	None	--	143	--	1,588	11.1	66	10.7	1,515	7	b/
Golden hamster	Captan	2,500†	4	6-10	49	12.2	23	6.8	25	1	
Golden hamster	Captan	1,500	6	6-10	54	9.0	14	6.7	40	0	
Golden hamster	Captan	1,000	4	6-10	44	11.0	4	10.0	40	0	
Golden hamster	Captan	500	2	6-10	25	12.5	0	12.5	25	0	
Golden hamster	Captan	1,000‡	6	7 or 8	64	10.7	36	5.8	20	8	
Golden hamster	Captan	750	7	7 or 8	76	10.9	11	10.4	55	10	
Golden hamster	Captan	600	5	7 or 8	64	12.8	12	10.4	48	4	
Golden hamster	Captan	500	10	7 or 8	122	12.2	14	10.9	103	5	
Golden hamster	Captan	400	8	7 or 8	93	11.6	6	10.9	87	0	
Golden hamster	Captan	300	9	7 or 8	115	12.8	5	12.3	101	9	
Golden hamster	Captan	200	3	7 or 8	40	13.3	5	12.0	35	0	

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* Daily intake.

† Total dose administered as five small daily doses.

‡ Single dose.

a/ Kennedy et al., *op. cit.* (1968).

b/ Robens, *op. cit.* (1970).

Using a slightly different approach, Robens (1970) compared the teratogenic potency resulting from single administration with the commonly recommended multiple administration throughout organogenesis. Captan at 200 to 1,000 mg/kg body weight was administered to pregnant hamsters either on the seventh or eighth day of gestation or for five consecutive days of gestation (days 6 through 10). Maternal mortality resulted from many of these levels. Terata from single administration included defects of the head, axial skeleton, limbs and viscera. As was shown in Table 9, the most highly teratogenic levels, calculated as percentage of implantation sites resulting in terata, was for captan at 1,000 mg/kg given as a single dose during the critical period of organogenesis (7 or 8 days). With multiple administration of each compound, litters were apparently normal at the low levels, while at the high levels maternal and fetal deaths and some decrease in fetal size occurred. No anomalies, such as resulted from a single administration, were found.

Rats - The teratogenic activity of captan in rats was studied by Kennedy et al. (1968). The results of feeding daily doses of 0, 50, 100 and 250 mg/kg body weight on days 6 through 15 of gestation and 500, 1,000 and 2,000 mg/kg body weight on days 8 through 10 of gestation are shown in Table 10. No teratogenic effects were seen at any dose rate through 500 mg/kg body weight. Teratogenic effects were observed only at the highest rates fed (1,000 and 2,000 mg/kg body weight). The terata observed were in the form of subdermal hematomas and umbilical hernia. One subdermal hematoma was observed in a control fetus. There was a slight reduction in weight of the normal fetuses produced by rats fed at the 2,000-mg/kg body weight level (4.5 g as compared with 4.8 g in the controls).

Mice - A mouse study was reported in an abstract by Kennedy et al. (1972).[1] Swiss white mice treated from gestation days 6 through 14 failed to show a teratogenic response to captan doses up to 100 mg/kg body weight.

The U.S. Health, Education and Welfare Department (1969)[2] reported that 100 mg/kg captan in Dimethyl Sulfoxide (DMSO) caused an increase in the proportion of abnormal litters and proportion of abnormal fetuses per litter in the C57BL/6 mouse. The level of statistical significance was .01. When captan was given to the same strain of mouse in honey or when given in DMSO to the AKR mouse, no anomalies were noted at 100 mg/kg.

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[1] Kennedy, G. L., J. F. Vondruska, O. E. Fancher, and J. C. Calandra, "The Teratogenic Potential of Captan, Folpet, and Difolatan," Teratology, 5:259 (1972).

[2] U.S. Health, Education and Welfare Department, "The Report of the Secretary's Commission on Pesticides and their Relationship to Environmental Health," Table 1, p. 670-671; Table 3, p. 673 (December, 1969).

Table 10. TERATOGENIC ACTIVITY OF CAPTAN IN RATS

Compound	Oral dose (mg/kg)	Number of pregnant females	Dosed, gestational days	Total number of implantations	Number of resorptions	Average litter size	Number of normal fetuses	Number of terata
Corn oil (control)	500*	10	6-15	126	3	12.3	122	1(0.8%)
Corn oil (control)	500	7	8-10	80	2	11.1	78	0
Captan	50	6	6-15	79	2	12.8	77	0
Captan	100	7	6-15	86	4	11.7	82	0
Captan	250	5	6-15	49	4	9.0	45	0
Captan	500	5	8-10	58	10	9.6	48	0
Captan	1,000	5	8-10	63	4	11.8	56	3(5.1%)
Captan	2,000	5	8-10	60	0	12.0	58	2(3.3%)

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* Daily oral dose.

Data from Kennedy et al., op. cit. (1968).

Avian Embryotoxicity - Verrett et al. (1969)[1] states that, "captan is indeed teratogenic in the developing chicken embryo." In this study, captan was injected directly into either the yolk or air cell of fresh fertile eggs at dose levels ranging from 0 to 20 ppm. Of a total of 1,292 eggs injected, 101 malformations (7.81% of total) were observed. Of the 101 abnormalities observed, 26 were in the head region, 31 in wing structure, 19 in leg structure, and 25 malformations of the lower body. Although it is concluded that captan is highly teratogenic, these studies were performed by egg injection and are atypical with respect to absorption of captan through the egg membrane during egg formation in the chicken. Actual feeding studies with captan (Verrett et al., 1969) indicate that captan is not absorbed through the egg shell membrane during egg production and no teratogenic effects can be observed.

In one study a group of five male and 18 female white leghorn chickens were fed a diet containing 0 or 2,300 ppm (equivalent to 75 mg/kg body weight) technical captan for 6 weeks. The birds were observed for body weight effects, food consumption, behavioral reaction, and egg production. Eggs collected during days 29 through 39 were incubated to determine the extent of hatchability and the presence of any effects on the chicks. No adverse effects were noted (Palazzolo, 1966).[2]

A summary of teratogenic studies reviewed in this section is given in Table 11.

Behavioral Effects

The review of the literature did not reveal any reports on adverse behavioral effects of captan.

Toxicity Studies with Tissue Cultures

Legator et al. (1969)[3] made a study of the mutagenic effects of captan. In this study, cell growth was evaluated. A heteroploid human embryonic cell line L/32 was used. Only a slight reduction of growth was obtained with 3 ppm captan. At the 4-μg/ml level, growth was severely inhibited for the initial 48 hr. After 48 hr, the cells recovered from captan treatment.

Mutagenic Effects

The Durham and Williams (1972) report has been used as the basis for this section dealing with investigations of captan's mutagenic effects.

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[1] Verrett, M. J., M. K. Mutchler, W. F. Scott, E. F. Reynaldo, and J. McLaughlin, "Teratogenic Effects of Captan and Related Compounds in the Developing Chicken Embryo," Ann. N. Y. Acad. Sci., 160:334-343 (1969).

[2] Palazzolo, R., Report on Captan, Industrial Bio-Test Laboratories, unpublished report, Northbrook, Illinois (1966).

[3] Legator, M. S., F. J. Kelly, S. Green, and E. J. Oswald, "Mutagenic Effects of Captan," Ann. N. Y. Acad. Sci., 160:344-351 (1969).

Table 11. SUMMARY OF TERATOGENIC INVESTIGATIONS WITH CAPTAN

Test animal	Results	Reference
Monkey	No fetal abnormalities or abortions when dosed with 10-75 mg/kg captan on days 21-34 of gestation.	a/
Monkey	No fetal abnormalities when dosed with 6.25-25 mg/kg captan on days 22-32 of gestation. Fetal mortality in three of seven monkeys at 25-mg/kg level.	b/
Rabbit (NZ)+	No fetal abnormalities with 80 mg/kg captan on days 7-12 of gestation. Four resorptions of 43 implantations (no significant difference compared to control).	c/
Rabbit (DB)*	No fetal abnormalities with 75 mg/kg captan on days 6-16 of gestation. One resorption in 43 implantations.	d/
Rabbit (NZ)+	No fetal abnormalities with 18.75-75.0 mg/kg captan on days 6-18 of gestation. Thirty-three resorptions in 39 implantations at 75 mg/kg.	d/
Rabbit	Nine malformed individuals from 75 implantation sites at dose level of 75 mg/kg. Malformations included deformed limbs, cleft lip, and fused upper lip.	e/
Dog	Daily captan dosage throughout gestation was 15, 30, or 60 mg/kg. 15 mg/kg gave 18.2% stillborn and one abnormality; 30 mg/kg gave 20.6% stillborn and three abnormalities; 60 mg/kg gave 4.5% stillborn and three abnormalities.	f/
Dog	Captan, up to 60 mg/kg/dog throughout gestation produced no signs of teratogenicity or embryotoxicity	g/
Hamster	Incidence of terata in test groups (125-1,000 mg/kg on gestation days 1-15) no higher than control group. Resorption incidence increased significantly at 1,000 mg/kg.	d/
Hamster	Single captan injection of 750 and 1,000 mg/kg on day 7 or 8 of gestation gave 13.7 and 22.9% fetal abnormalities, respectively Respective fetal resorptions were 17.1 and 57.8%. Multiple administration of 100-500 mg/kg/day on days 6-10 of gestation gave only one terata at highest dose. Resorption rate increased with dose.	h/
Rat	No fetal abnormalities at dosages 50-250 mg/kg on gestation days 6 to 15. At 1,000 and 2,000 mg/kg on gestation days 8-10, 3.3 and 5.1% terata occurred, respectively.	d/
Mouse	Captan levels up to 100 mg/kg on gestation days 6-14 showed no teratogenic response.	i/
Mouse	100 mg/kg captan in DMSO, produced terata in one species while the same dose in DMSO to another species was negative; captan in honey was also negative.	j/
Chicken	Injection of captan into egg yolk or air sac at up to 20 ppm resulted in 101 abnormalities (7.8% of total). Feeding captan to chickens resulted in no terata.	k/

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* DB - Dutch belted.
+ NZ - New Zealand white.
a/ Vondruska et al., op cit. (1971).
b/ Courtney (1968). Quoted in Anon., FAO/WHO report, op. cit., (1970).
c/ Fabro et al., op. cit. (1965).
d/ Kennedy et al., op. cit. (1968).
e/ McLaughlin et al., op. cit. (1969).
f/ Earl et al., op. cit. (1974).
g/ Kennedy et al., op. cit. (1972).
h/ Robens, op. cit. (1970)
i/ Kennedy et al., op. cit. (1972).
j/ U.S. Health, Education and Welfare Department, op. cit. (1969).
k/ Verrett et al., op. cit. (1969).

Mutagenesis is defined as the study of mutations or an inherited change in the genetic material of an organism. The change may be a chemical transformation of a gene so that its function is altered, or it may be a chromosomal alteration. The mutations of most interest are those transmitted by way of sperm or ovum to the next generation. Roughly, the methodology can be divided into four categories:

1. Submammalian tests
    a. Bacterial
    b. _Neurospora_ spp.
    c. _Drosophila_ spp.
2. Cytogenicity of mammalian cell culture
3. Host-mediated assay test
4. Mammalian tests
    a. Specific locus test
    b. Dominant lethal test

There are a number of opinions as to what type of test should be used to estimate mutagenesis. Epstein (1970)[1] felt that submammalian systems were not of great value. Epstein and Shafner (1968)[2] advocated the dominant lethal test.

Durham and Williams (1972) quoting Jacobson (1971) reported that 275 chemicals had been tested for mutagenicity by the dominant lethal test, and seven gave positive results. One hundred compounds had been evaluated by the host-mediated assay, and six positive results were obtained.

Legator (1970)[3] addressed the value of mutagenicity tests by listing some contributions from the Food and Drug Administration research: (1) characterization of the natural occurring mycotoxin (aflatoxin) as a mutagenic agent; (2) determination of the _in vivo_ cytogenetic effects of cyclohexylamine, a metabolite of cyclamate; (3) characterization of captan as a mutagenic agent; and (4) the induction of the dominant lethal effects of DDT. These compounds reveal an interrelationship between mutagenic, carcinogenic, or teratogenic effects. Aflatoxin is teratogenic, carcinogenic, and mutagenic. Cyclamate has been shown to induce bladder tumors. Captan is teratogenic in laboratory animals, and DDT produces tumors in animals. Legator stated that carcinogenic agents are usually mutagenic, but the converse is not always true.

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[1] Epstein, S. S., "Control of Chemical Pollutants," _Nature_, 228:816-819 (1970).

[2] Epstein, S. S., and H. Shafner, "Chemical Mutagens in the Human Environment," _Nature_, 219:385-387 (1968).

[3] Legator, M. S., "Chemical Mutagenesis Comes of Age," _J. Hered._, 61(5): 239-242 (1970).

Legator et al. (1969) evaluated the mutagenic activity of captan in bacteria. The bacteria used in the study were *Escherichia coli* SD4-73 strains. The bacteria were grown for 24 hr in an aerated broth culture, supplemented with 100 µg of streptomycin per milliliter. The washed cells were added to soft agar; and the seeded layer was added to 15 ml of a 2% nutrient agar base with and without the antibiotic. A small disk was placed on the surface of the media and moistened with dimethyl sulfoxide containing the test chemical. With the concentration of 250 µg per assay disk, the mutants were increased sixfold. When the concentration of captan was raised to 1,000 µg per disc a tenfold increase of mutants occurred over the control. An *E. coli* thymine-dependent strain was used as a test organism and 1,000 µg of captan per assay disk brought about a tenfold increase in the mutants over the control.

Ficsor and Nii Lo Piccolo (1970a and 1972)[1,2] tested 14 pesticides purchased from a hardware store for mutagenicity in *E. coli* and *Salmonella typhimurium*. Two of the pesticides were mutagenic and both of them contained captan (15% and 5%). Their test procedure was a rather simple one, about 1 to 2 x 10^8 bacteria were plated on minimal plates. The plates were dried and spotted with pesticides and the mutagen nitrosoguanidine. Among the strains tested cys B-12 in *S. typhimurium* responded with the highest frequency of reversions.

Ficsor and Nii Lo Piccolo (1970b)[3] made a study of the effect of heating to sterilization temperatures on captan mutagenicity. They used *E. coli* and cys mutant of *S. typhimurium*. The heat treatment of the pesticide was accomplished by making a 1:10 suspension of the pesticide in sterile distilled water. The suspension was divided into three parts: (1) to stand at room temperature; (2) steam sterilization for 15 min, which is about 100°C; and (3) autoclaved 15 min at 15 lb pressure. In the latter situation the temperature rose to about 121°C. After cooling, the pesticides were placed on the plates, and reverted colonies were counted. In the lac mutant the autoclaved pesticide induced 21 times fewer reversions than the pesticide kept at room temperature. The steam-sterilized pesticide induced five times fewer reversions than the room temperature check.

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[1] Ficsor, G., and G. M. Nii Lo Piccolo, "Captan-Induced Reversions of Bacteria," *Newlett. Environ. Mutagen. Soc.*, 3:38 (1970a).

[2] Ficsor, G., and G. M. Nii Lo Piccolo, "Survey of Pesticides for Mutagenicity by the Bacterial-Plate Assay Method," *Environ. Mutagen. Soc.*, 6:6-8 (1972).

[3] Ficsor, G., and G. M. Nii Lo Piccolo, "The Effect of Temperature on the Mutagenicity of Captan," *Environ. Mutagen. Soc.*, 3:38 (1970b).

Malling and deSerres (1970)[1] tested captan on Neurospora crassa in a series of pilot experiments to see if they could induce forward mutations in the ad-3 region of a two-component heterokaryon and reverse mutations in a series of test strains. They were able to obtain positive evidence of mutagenesis of captan in the forward mutation system, but not in the reverse mutation system.

Siebert et al. (1970)[2] used Saccharomyces cerevisiae to test 14 fungicides for genetic activity. Their test system involved the induction of mitotic gene conversion at two different loci and cytoplasmic respiratory deficient mutants. Captan was found to be a weak agent for involving mitotic gene conversion and did not induce cytoplasmic mutation.

Clarke (1971)[3] used a mutational system of reversion to tryptophan independence in the Escherichia coli B/r ochre auxotrophic mutant WWP-2. Both the repair competent and excision repair deficient derivatives of this strain were used in an effort to determine whether or not the mutagenic activity of a pesticide was dependent on excision repair. Three formulations of captan were tested. These chemicals markedly brought about mutagenic activity causing an approximate 20-fold increase in revertant numbers in the excision repair competent strain and approximately 100-fold in the excision repair deficient strain.

Bridges et al. (1972a)[4] worked with a number of repair-deficient strains of Escherichia coli. These strains provided a sensitive assay system for the mutagenic activities of chemicals and also permit useful information to be obtained about the characteristics of the mutagenic process. Using the various strains in simple spot testing experiments, they observed mutagenic actions occurring in five strains. They showed that a substantial part of the mutagenic activity of the fungicide captan is due to excisable DNA damage mediated by a volatile breakdown product. They felt that the mutagenic properties of captan are in essence those of one or more alkylating agents.

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[1] Malling, H. V., and F. J. deSerres, "Captan--A Potent Fungicide with Mutagenic Activity," Environ. Mutagen. Soc., 3:37 (1970).

[2] Siebert, D., F. K. Zimmermann, and E. Lemperle, "Genetic Effects of Fungicides," Mutat. Res., 10:533-543 (1970).

[3] Clarke, C. H., "The Mutagenic Specificities of Pentachloronitrobenzene and Captan, Two Environmental Mutagens," Mutat. Res., 11(2):247-248 (1971).

[4] Bridges, B. A., R. P. Mottershead, M. A. Rothwell, and M. H. L. Green, "Captan Mutagenesis of Repair-Deficient Strains of Escherichia coli," Environ. Mutagen. Soc., 6:9 (1972).

Seiler (1973)[1] made a survey of some 30 pesticides for their propensity for mutagenesis. They made their evaluations in five different strains of *Salmonella*. Captan proved to be mutagenic in two of these strains. The rating given by the authors was 2+ which they considered medium. Captan has been shown to be a mutagenic substance through its alkylating potency (Legator, 1969; Clarke, 1971). Investigations have failed to disclose the similar effect in *Drosophila* (Mollet, 1973)[2] as well as in the dominant lethal test in mice (Anon., FAO/WHO report, 1970, quoting Arnold, 1967).

Buselmaier et al. (1972)[3] evaluated 16 chemicals in host-mediated and dominant lethal tests. None of the compounds proved to be mutagenic in the dominant letnal test. Captan was definitely mutagenic in the host-mediated assay.

Kramers and Knaap (1973)[4] investigated the mutagenic effects of captan in *Drosophila melanogaster*. They administered pure captan by injection into the abdomen of 4-day-old males (approximately 0.2 μg/ml) or by continuous feeding of larvae from the first instar until the adult stage. They checked three types of induced genetic damage: (1) complete and mosaic sex-linked recessive lethal mutations in male germ cells; (2) II to III translocations in male germ cells; and (3) dominant lethal mutations in male and female germ cells. In the sex-linked recessive tests, the frequency obtained in the captan series appeared to be rather high, but the pooled data (19 lethals in 4,360 chromosomes tested) did not differ significantly at the 5% level from the control (pooled 24 lethals in 9,155 chromosomes tested). No translocations were found in the total of 1,271 gametes after a larval feeding of captan at concentrations of 0.3 and 1%. And none were observed in the total of 2,172 gametes tested after injection of the same substance. No evidence was produced to indicate the induction of dominant lethal mutations. They concluded that their results failed to demonstrate mutagenic activity of captan under the conditions employed although the possibility was not ruled out that a very mild effect may exist. The investigators' interpretation was that possibly captan is destroyed before it reaches the gonads in an effective concentration.

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[1] Seiler, J. P., "A Survey on the Mutagenicity of Various Pesticides," *Experientia*, 29:622-623 (1973)

[2] Mollet, P., "Untersuchungen uber Mutagenitat and Toxizitat von Captan bei Drosophila," *Mutat. Res.*, 21:137-138 (1973).

[3] Buselmaier, W., G. Rohrborn, and P. Propping, "Mutagenitats-Untersuchungen mit Pestiziden im Host-mediated assay und mit dem Dominanten Letaltest an der Maus," *Biol. Zbl.*, 91:311-325 (1972).

[4] Kramers, P G. N., and A. G. A. C. Knaap, "Mutagenicity Tests with Captan and Folpet in *Drosophila melanogaster*," Mutat. Res., 21: 149-154 (1973).

Mollet (1973) tested captan for its mutagenicity in adult males of Drosophila melanogaster. He determined mutagenicity from the frequency of sex-linked recessive lethal in pre- and post-meiotic germ cells. It was found that captan was not mutagenic at low nontoxic or at high toxic concentrations. Even in combination with the solvent dimethyl sulfoxide, captan was not mutagenic. The results were explained by the assumption that captan is inactivated before it reaches the germ cells.

Legator et al. (1969) evaluated the mutagenic activity of captan in a cell line derived from human embryonic lung cells and from the kidney of the kangaroo rat.

The embryonic lung cell line was a heteroploid human embryonic cell line L-132. Growth was reduced slightly by 3 μg/ml of captan. At the 4-μg/ml level minimal growth occurred up to 48 hr. After 48 hr, the cells recovered from captan treatment. When the concentration was in excess of 5 μg/ml, no growth occurred. It is noteworthy that 100 μg/ml of tetrahydrophthalimide and phthalimide were nontoxic. Initial inhibition of mitosis by captan at the time of incubation was found at 3 and 4 μg/ml.

Chromosome studies were made and the procedure was the same for mitotic inhibitions. The cells were exposed to captan after 40 hr of incubation. After the addition of captan, cells were removed and metaphase cells examined for chromosome effects. There appeared to be increases in breaks in 2 to 4 hr after the addition of captan and the increase persisted through 24 hr. These breaks were mainly of the chromatid type with a few exchange figures found in the 24-hr time interval.

The kangaroo rat cell line was grown in monolayer cultures, at 37°C in an atmosphere of 3% carbon dioxide. After 16 hr exposure to 1 μg/ml captan, there was approximately 3% mitosis; 5 μg/ml produces 1% mitosis. The percentage of chromosome breaks rose from 10% at 1 μg/ml of captan to 70% at 10 μg/ml of captan.

Epstein and Shafner (1968) studied the mutagenicity of a wide variety of environmental pollutants using mice as a screening element. In general, the LD_{50} doses were selected for testing and they rated the reaction of the chemicals in terms of a mutagenic index (MI). This index reflected the incidence of dominant lethal mutations, and was calculated by the following formula:

$$MI = \frac{\text{deciduomata + late deaths}}{\text{total implantations}} \times 100.$$

Captan was evaluated at two dosage levels (500 and 9 mg/kg), and it was administered both intraperitoneally for low doses, and orally for higher doses. They bred 21 females in one instance and 18 in another, and the percentage pregnancies were 95% and 83%, respectively. The average number of implants were 10.5 and 11.4. The MI values for captan were in the control range.

A number of structurally related compounds, captan, captafol, folpet and thalidomide were studied in two types of mutagenic tests: the dominant lethal study in mice and the host-mediated assay in rats using a histidine auxotroph of Salmonella typhimurium (Kennedy et al).[1] Doses of captan in the dominant lethal study were 3 and 6 mg/kg injected IP once and in the host-mediated assay, 125 and 250 mg/kg by intubation for 14 days. None of the compounds were positive in either test system.

Captan, 3.5 or 7.0 mg/kg, was injected into male mice prior to mating with untreated females. One positive control was methylmethane sulfonate, while actinomycin D was also used as a positive control, since it has been reported to induce chromosomal breaks in vitro similar to those seen with captan (Arnold et al. 1967)[2]. No dominant lethal mutations were noted.

Collins (1972a)[3] injected technical grade captan into male rats and mice. The administrations were given either intraperitoneally IP in doses of 2.5, 5.0, or 10.0 mg/kg/day for 5 days or by oral intubation doses of 50, 100, or 200 mg/kg/day for 5 days. An increase in the mean number of early fetal deaths per pregnancy was seen in rats during the first 7 weeks after IP administration of captan at the highest dose level, but this increase was not statistically significant. Similar effects were obtained with intubation. There were increases in the mean number of early deaths at all dose levels but were statistically significant only after the fourth week after intubation with 100 mg/kg/day and weeks 1, 2, and 5 with 200 mg/kg/day. Mutagenic damage appeared to be slight. Mutagenic effects as measured by the increase in the mean number of early fetal deaths per pregnancy were visible in mice after IP treatment of captan at the highest dose level for the first 7 weeks after implantation. But the increase was only significant for weeks 4 and 5. Increases were notable at the highest dosage levels for the first 5 weeks after oral intubation of captan, but no statistically significant increases were found after the second week. At all levels of IP treatment, captan produced no significant increase in the percentage of litters with one or more early deaths and only one significant increase in the percentage of the litters with two or more early deaths. With oral intubation, similar results were obtained. Even at the highest dose levels of intraperitoneal or orally administered captan no dominant lethal mutants were detected by any decrease in total implantations per pregnant female.

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[1] Kennedy, G., D. Arnold and M. Keplinger, "Mutagenic Studies with Captan, Captofol, Folpet and Thalidomide," unpublished report, Industrial Bio-Test Laboratories, Northbrook, Ill. (undated).

[2] Arnold, D., R. Kodras, and O. Francher, "Mutagenic Study on Captan," unpublished report by Industrial Bio-Test Laboratories for Chevron Chemical Co., Richmond, Calif. (1967).

[3] Collins, T. F. X., "Dominant Lethal Assay. I. Captan," Food Cosmet. Toxicol., 10:353-361 (1972a).

A summary of the investigations of the mutagenic effects of captan is presented in Table 12.

Oncogenic Effects

It is advisable that the route of the administration for the testing of chemicals for carcinogenesis should be by the same exposure route as used for humans, for example, as in exposures from residues and food (Durham and Williams, 1972).

Steckerl and Turner (1965)[1] had found in early experiments that the extracts of seeds inhibited the development of mouse ascites carcinoma and this inhibitory action had been traced to the presence of captan, which had been used as a seed treatment. These investigators injected white Swiss mice with 0.15 g/kg of captan intraperitoneally for 14 days, and these animals had been inoculated 1 day before injection with 2×10^6 ascites tumor cells. Dosages of captan above this level were found to be too toxic. The mean survival of mice inoculated with ascites tumor cells was increased from 26 to 80 days by the injection of the captan. They also noted that all the mice treated with captan, on autopsy, had solid masses apparently originating from the injection site in the abdominal wall. No histopathological examination of the masses was made.

Innes et al. (1969) investigated the tumorigenicity of 130 compounds in mice. They used two hybrid strains of mice of both sexes with 18 animals per group. Maximum tolerated doses were either administered by single subcutaneous injection or continuous oral administration. For their tumorigenicity test, the dose was given by stomach tube beginning when the mice were 7 days of age. The same absolute amount of each compound was given each day until the mice were 4 weeks old. Captan was given at a daily dosage of 215 mg/kg in a vehicle which is equivalent to about 560 ppm in a 0.5% gelatin vehicle. The dose was not adjusted according to weight. As the mice were weaned at 4 weeks of age, captan was added directly to the diet at 560 ppm. No vehicle was used when captan was fed in the diet. The test ran for 18 months, and there was no significant increase in tumors in the animals fed captan as compared with the controls.

Swiss white mice were fed technical captan at doses of 0, 3,750 or 7,500 ppm in the diet which approximated 0, 560 or 1050 mg/kg/day. N-Nitroso diethylamine (10 ppm) was the positive control. The positive control caused focal hyperplastic changes in the livers of both sexes and neoplastic lesions in the liver, lung and forestomach of the females. Captan did not cause any gross or microscopic changes nor did it cause increased mortalities. Other parameters besides histology and gross observations were not measured. (Reyna et al. 1973).[2]

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[1] Steckerl, F., and M. L. Turner, "Effect of Captan on the Mouse Ascites Tumor of Ehrlich," Nature, 206:839 (1965).

[2] Reyna, M., G. Kennedy, and M. Keplinger, Eighteen-Month Carcinogenic Study with Captan Technical in Swiss White Mice, unpublished report, Industrial Bio-Test Laboratories, Northbrook, Ill. (April, 1973).

Table 12. SUMMARY OF MUTAGENIC INVESTIGATIONS WITH CAPTAN

System	Organism or tissue	Results	Reference
Bacteria	*Escherichia coli* SD4-73 strains	Mutations were observed	a/
	Escherichia coli NG 422 and YA 482	Mutagenic	b/
	Salmonella typhimurium *CYS*-(*CYS* B12) *LEU*-(AP 517, 5BU 504)	Mutagenic	c/
	Neurospora crassa	Mutagenesis in forward mutation system	d/
	Neurospora crassa	None in reverse mutation system	d/
	Escherichia coli *B/r ochre auxotrophic* Mutants WWP-2 (her+ and her-)	Markedly mutagenic in excision repair deficient and competent strain	e/
	Escherichia coli WP2 *TRP* (ochre) WP2 *uvrA*, CM 561 *exrA*, CM 571 *recA*, CM 611 *uvrA*, *exrA*	Mutagenesis occurred in five strains	f/
	Salmonella strains G46, TA1530, TA1531, TA1532, TA1534	Mutagenic in two strains	g/
	Salmonella typhimurium G46 His-	Mutagenic in host-mediated assay	
	Salmonella typhimurium G46 His-	Nonmutagenic in host-mediated assay	h/
Yeast	*Saccharomyces cerevisiae*	Weak agent for inducting mitotic gene conversion	i/
	Diploid strain DY Haploid MA20: α, *gal*2, *ade*2-2, trp5-12 - *leu*I; MD 20: α +, *ade*2-I, trp5-27 - +	No induced cytoplasmic mutation	
Tissue culture	Embryonic lung ceil human L-132	Above 5 mg/ml no growth occurred Break in chromosomes occurred	a/
	Rat - kangaroo cell line	Mitosis resumes at 1 μg/ml; 70% chromosomes break at 10 μg/ml	a/
Drosophila	*Drosophila melanogaster*	Failed to demonstrate mutagenic activity using sex-linked recessive lethal, II-III translocations and dominant lethal tests	j/
	Drosophila melanogaster	No mutagenic effects by sex-linked recessive lethal tests	k/
Mice	Mice, NMRI strain	Nonmutagenic in dominant lethal test	l/
	Swiss mice, CD-1	Mutation index (dominant lethal test) same as controls	l/ m/
	CR Mice	Nonmutagenic in dominant lethal test	n/
	Swiss white mice	Nonmutagenic in dominant lethal test	o/
Mice and rats	Osborne Mendel rats CBA-J mice	No dominant lethal mutants were detected	p/

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a/ Legator et al., *op. cit.* (1969).
b/ Ficsor and Nii Lo Piccolo, *op. cit.* (1970a).
c/ Ficsor and Nii Lo Piccolo, *op. cit.* (1972).
d/ Malling and deSerres, *op. cit.* (1970).
e/ Clarke, *op. cit.* (1971).
f/ Bridges et al., *op. cit.* (1972).
g/ Seiler, *op. cit.* (1973)
h/ Kennedy et al., Industrial Bio-Test Laboratories, unpublished report, *op. cit.*
i/ Siebert et al., *op. cit.* (1970).
j/ Kramers and Knaap, *op. cit.* (1973).
k/ Mollet, *op. cit.* (1973).
l/ Buselmaier et al., *op. cit.* (1972).
m/ Epstein and Shafner, *op. cit.* (1968).
n/ Kennedy et al., Industrial Bio-Test Laboratories, unpublished report, *op. cit.*
o/ Arnold et al., *op. cit.* (1967).
p/ Collins, *op. cit.* (1972a).

In a chronic study[1] with rats of 104 weeks duration, 10 female and 10 male rats were placed on each of four diets, basal, basal plus 0.1% captan, basal plus 0.5% captan, and basal plus 1.0% captan. At the 24th week half of the animals were placed on 1% recrystallized captan. At the time of death or sacrific the following observations were made:

Diet	Tissue Abnormalities
Control	1 Male - Intragastric fibroma-ulcerating 1 Female - Adeno fibroma - breast
0.1% Captan	1 Male - Benign liver hepatoma 1 Female - 2 Benign cystic breast tissues 1 Benign papillary cyst adenoma 1 Breast adenoma
0.5% Captan	1 Male - Interstitial adenoma of the testes 1 Male - Benign liver hepatoma 4 Females - 1 Benign liver hepatoma 1 Benign hurthe cell adenoma thyroid 2 Hyperplastic breast tissues 2 Benign papillary cyst adenofibromas of the breast
Diet	1 Benigh fibroma or reticular cell tumor - marked hyperplasia and malignant potentialities 1 Lutein cyst of ovary 1 Benign fibroma
1.0% Captan	None

Preliminary data indicates an increase in lung tumors in female Swiss mice receiving 11 doses of approximately 20 mg/kg captan for 22 days. Captan was administered either intraperitoneally or by gavage (Roserkranz, 1974)[2].

Effects on Man

There was little information available on the acute and subacute toxicity of captan, the symptoms of its poisoning, dermal and inhalation effects, the occupational hazards posed by the use of captan in crop application, and the hazards that might be involved in its manufacture. One study in an article by Durham and Williams (1972) cites an Idaho Pesticide Community Study, EPA. The study reported no lymphocyte chormosome abberations could be attributed to captan among workers in a formulation plant.

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[1] Captan Reports, EPA Pesticide Petition Nos. 15 and 124, Section C.

[2] Rosenkranz, H. S., Department of Microbiology, Columbia University, N.Y.C, personal communication (1974).

Accidents involving captan, however, have been more fully reported. Preliminary data from the EPA Pesticide Accident Surveillance System (PASS) show that captan was cited in 33 episodes (involving humans, animals, and plants as well as area contamination) for the period of 1972 through January 1974. Eleven of these cases were reported for 1973 (captan was the 39th most frequently cited pesticide for 1973).

The available accident data does not establish a pattern between captan and any specific use. Ten of the 33 reported episodes, however, did involve possible intoxication of children from home and garden products (treated flowers and vegetable seeds, tomato dust, etc.).

Summary

Reproduction - In reproductive studies with rats, as much as 1,000 ppm of captan was fed through to two generations (two litters per generation) without any effect on fertility, gestation, viability or lactation indices. In the third generation, the lactation index was suppressed slightly. When captan was given in daily doses of 6 to 57 mg/kg, sperm motility was decreased. The same observation was made for mice (daily dosage 2.5 to 20 mg/kg). In another test, mice received 50 or 100 mg/kg for 5 days. The fertility index was depressed at both levels. The weaning weights were decreased in the first litter of the second generation.

Teratology - Single and multiple doses (200 to 1,000 mg/kg) of captan have been given to pregnant hamsters on the seventh and eighth day or on days 6 through 10 of gestation. Anomalies occurred after single dose administration; 13.7% of the young were deformed at a dose level of 750 mg/kg given on day 7. The dose resulted in 22% dam mortality. After a dose of 500 mg/kg was given on days 6 through 10 of gestation, the young were normal. At higher levels, fetal death and small fetuses were observed, but there were no anomalies.

In another test, hamsters were given 125, 250, 500 and 1,000 mg/kg of captan each day for the first 15 days of gestation. There were no more abnormal effects in the test group that received 1,000 mg/kg than in the control group.

There have been two reports where rabbits received 80 mg/kg and 75 mg/kg during gestation (days 7 through 12 and days 6 through 16) and no malformed fetuses were produced. Conversely, it has been reported that nine malformed fetuses were found in 75 implants in nine pregnant rabbits.

In one investigation in rats, high levels of captan (50 to 500 mg/kg body weight) did not produce a significant increase in the number of abnormalities (395 fetuses were observed). Abnormalities were observed at the next highest levels of 1,000 and 2,000 mg/kg.

No teratogenic effects were observed in monkeys receiving daily doses of 6.25, 12.5 or 25 mg/kg of captan. Fetal mortality was high at the 25 mg/kg level.

An incidence of 7.81% malformations (of the total number of embryos tested) has been observed in chick embryos where the eggs were injected with 0 to 20 ppm of captan.

In tissue cultures, 4 mg/ml of captan severely inhibited growth for 48 hr. After that period, the cells recovered and normal growth ensued.

Mutagenesis - There are a number of investigations of mutagenic effects of captan. Mutations have been observed in bacteria (*Escherichia coli* and *Salmonella typhimurium*) and in fungi (*Neurospora crassa* and *Saccharomyces cerevisiae*). Concentrations of 250 µg of captan in contact with *Escherichia coli* produced a sixfold increase in mutants; a ten-fold increase was produced by 1,000 µg.

Captan produced positive evidence of mutagenesis in the forward mutation system and none in the reverse mutation system with use of *Neurospora crassa* as a test organism.

In one investigation with *Saccharomyces ceverisiae*, captan was found to be a weak agent for mitotic gene conversion and did not induce cytoplasmic mutation.

Captan has produced marked mutagenic activity in causing an approximate 20-fold increase in revertant numbers in the excision repair-deficient strain and approximately 100-fold increase in the excision repair competent strain using *Escherichia coli* B/r ochre auxotrophic mutant WWP-2.

It has been shown that a substantial part of the mutagenic activity of captan is due to excisable DNA damage mediated by a volatile breakdown product.

In one investigation, captan did not bring about sex-linked recessive lethal mutations, translocations or dominant lethal mutations in *Drosophila melanogaster*. Another investigator reported that captan was not mutagenic (sex-linked recessive lethal test) in *Drosophila melanogaster*. It was assumed that captan was inactivated before it could reach the germ cells.

Chromosome studies were made of a heteroploid human embryonic cell line exposed to captan. There was an increase in breaks in 24 hr after the addition of captan. The break persisted for 24 hr. The breaks were mostly chromatid types. In a kangaroo rat cell line, the percentage of chromosome breaks rose from 10% at 1 µg/ml to 70% at 10 µg/ml of captan.

Captan did not produce dominant lethal mutations when mice were injected intraperitoneally (single) with 3.5 and 7.0 mg/kg of captan. In other investigations with mice, the incidence of dominant lethal mutations was in the normal range.

Mutagenic effects have been observed in mice as measured by the increase in the mean number of early fetal deaths per pregnancy after intraperitoneal injection into the male of 10.0 mg/kg (5 days) during the first 7 weeks after implantation.

At the highest dose levels of intraperitoneally or orally administered captan, no dominant lethal mutants were indicated by a decrease in total implantations per pregnant female.

Oncogenesis - It has been shown that captan injected intraperitoneally increases the mean survival times of mice (from 26 to 80 days) that have been inoculated with ascites tumor cells. In addition, all the mice treated with captan were found to have developed solid masses at the site of injection into the abdominal wall. A histological evaluation to classify the observed masses as tumors was not made.

Captan has been administered to mice at a level equivalent to about 560 ppm in the diet for 18 months and there was no significant increase of tumors over the controls.

Information on the effects of captan on man relative to acute and subacute toxicity, and inhalation effects, or the possible occupational hazards involved in application or manufacture is limited.

In an EPA Pesticide Community study of possible chromosomal aberrations among workers in a captan formulating plant, no chromosomal damage was reported.

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART C. FATE AND SIGNIFICANCE IN THE ENVIRONMENT

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This section contains data on the environmental effects of captan, including effects on aquatic species, wildlife, and beneficial insects and interactions with lower terestrial organisms. Captan residues in soil are also discussed. The section summarizes rather than interprets data reviewed.

Effects on Aquatic Species

Fish -

Laboratory studies - Toxicity of captan to fish has been studied in some detail. The effects of captan on other aquatic organisms (with the exception of Daphnia magna) have not been as thoroughly examined.

Acute toxicity data for fish in terms of TL_{50}'s, LC_{50}'s, and single concentration exposure tests are summarized in Table 13.

The acute toxicity of captan for zebrafish larvae was demonstrated by Abedi and McKinley (1967)[1], who advocated the use of this species in a bioassay for the fungicide. The LC_{50} determined in this study was 0.67 ppm (90 min).

The death of zebrafish larvae from captan poisoning was reported to be always associated with an observable head injury in which the eyeballs, while still retaining connection with the optic tissues, appeared to be blown out of the sockets and the head was ruptured into lateral halves to give a bicephaleous appearance. The head injury reported for zebrafish larvae during captan poisoning is considered to be a specific response of this species (Abedi and McKinley, 1967; Abedi and Turton, 1968)[2]. Captan has not been reported to exhibit this toxicity effect for other fish.

Nishiuchi and Hashimoto (1969)[3] have reported the TL_m (median tolerance limit) for a 48-hr exposure to be 0.25 ppm for the common carp and 0.037 ppm for the goldfish.

Rainbow trout were reported by Holland et al. (1960)[4] to exhibit 50% mortality when exposed to captan for 72 hr at a concentration of 0.16 ppm in aerated freshwater. The smaller specimens were not as susceptible as were the larger (2.8-in. versus 4.8-in. trout), at an equal concentration of captan, but the condition of the smaller fish at the end of the experiment indicated that some damage was produced at less than 0.32 ppm captan.

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[1] Abedi, Z. H., and W. P. McKinley, "Bioassay of Captan by Zebrafish Larvae," Nature (London), 216:1321-1322 (1967).

[2] Abedi, Z. H., and D. E. Turton, "Note on the Response of Zebrafish Larvae to Folpet and Diofolatan," J. Assoc. Off. Anal. Chem., 51: 1108-1109. (1968).

[3] Nishiuchi, Y., and Y. Hashimoto, "Toxicity of Pesticides to Some Freshwater Organisms, "Rev. Plant Protec. Res., 2:137-139 (1969).

[4] Holland, G. A., J. E. Lasater, E. D. Neuman, and W. E. Eldridge, "Toxic Effects of Organic and Inorganic Pollutants on Young Salmon and Trout," Department of Fisheries Resource Bulletin No. 5, Washington, D.C., 136-139 (1960).

Table 13. TOXICITY OF CAPTAN TO FISH

Test species	Sex and age of animals	Toxicity calculation	Toxicity measured	Comments	Reference
Bluegills	Fingerlings	LC$_{50}$ (96 hr)	150 µg/l	Static system	b/
Bluegills	Mixed sex, 1.5 months	TL$_{50}$ (96 hr)	72 µg/l	Flow-through system	a/
Carp	Mixed sex, young	TL$_m$ (48 hr)	0.25 ppm	-	d/
Channel catfish	Fingerlings	LC$_{50}$ (96 hr)	77.5 µg/l	Static system	b/
Coho salmon	Fingerlings	LC$_{50}$ (96 hr)	56.5 µg/l	Flow-through system	b/
Fathead minnows	Mixed sex, 3.5 months	TL$_{50}$ (96 hr)	65 µg/l	Flow-through system	a/
Fathead minnows	Fingerlings	LC$_{50}$ (96 hr)	120 µg/l	Flow-through system	b/
Fathead minnows	Mixed sex	Toxicity, chronic (45 weeks)	Mortality at 29.5 and 63.5 µg/l	24% Mortality at 39.5 µg/l; 100% mortality at 63.5 µg/l	a/
Goldfish	Mixed sex, young	TL$_m$ (48 hr)	0.037 ppm	-	d/
Brook trout	Mixed sex, 1.5 months	TL$_{50}$ (96 hr)	34 µg/l	Flow-through system	a/
Cutthroat trout	Fingerlings	LC$_{50}$ (96 hr)	48.5 µg/l ($\bar{x}$ of 2)	Static system	b/
Lake trout	Fingerlings	LC$_{50}$ (96 hr)	51.0 µg/l	Flow-through system	b/
Lake trout	Fingerlings	LC$_{50}$ (96 hr)	75.2 µg/l	Static system	b/
Rainbow trout	Fingerlings	LC$_{50}$ (96 hr)	102 µg/l	Static system	b/
Rainbow trout	Mixed sex, young	72 hr toxicity exposure	Mortality at 0.32 ppm	50% Mortality at 32 ppm	e/
Zebrafish	Mixed sex, larvae	LC$_{50}$ (90 min)	0.67 ppm	-	c/

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a/ Hermanutz, R. O., L. H. Mueller, and K. D. Kempfert, "Captan Toxicity to Fathead Minnows (Pimephales promelas), Bluegills (Lepomis macrochinus), and Brook Trout (Salvelinus fontinalis)," J. Fish Res. Board Can., 30:1811-1817 (1973).

b/ United States Department of the Interior, Fish-Pesticide Laboratory, Columbia, Missouri, unpublished data (1968-1972).

c/ Abedi and McKinley, op. cit. (1967).

d/ Nishiuchi and Hashimoto, op. cit. (1969).

e/ Holland et al., op. cit. (1960).

The lethal threshold concentration (LTC) is considered by some investigators to be a better measure of acute toxicity than is the 96-hr TL_{50}. However, as can be seen in Table 14, the data of the Hermanutz et al. (1973) study shows good correlation (flow-through system) between the two toxicity measurements for fathead minnow, bluegill, and brook trout.

In an extension of their study Hermanutz et al. (1973) also examined the effect of static exposure to fathead minnows. Minnows placed in the test tanks immediately after introduction of a static concentration of 550 μg of captan per liter died within 8 hr. A second group placed in the same chamber 3 hr after introduction of the toxicant lived without any apparent harmful effects (observed for 10 days) indicating that breakdown of captan was rapid in the water used in these tests.

Mauck (1972)[1/] compared captan toxicity to several fish species using two experimental water systems: (1) a static system and (2) a flowing system. The results (Tables 15 and 16) indicated that in a static system, where an initial level of captan might decrease with time because of hydrolysis, etc., the toxic effect for fish diminishes rapidly. For example, for Coho salmon, the 96-hr LC_{50} in the static system was 137 μg/liter; but in a flowing system where the captan level was held constant, the LC_{50} was 56.5 μg/liter.

Hermanutz et al. (1973) studied captan toxicity to fathead minnows. Growth and survival were not adversely affected by chronic exposure to 3.3, 7.4, or 16.8 μg of captan per liter of water. These relationships are illustrated in Table 17.

Statistical evaluation of the data showed the maximum acceptable toxicant concentration (MATC) to be between 39.5 and 16.8 μg/liter of water. All but one of the fish died at a captan concentration of 63.5 μg/liter in the 51-day period. However, the survival of fish at the other concentrations did not differ significantly from the controls after 51 days and 45 weeks of exposure.

[1/] Mauck, B., Annual Progress Report: 1972 (unpublished data), Fish-Pesticide Research Unit, Bureau of Sport Fisheries and Wildlife, La Crosse, Wisconsin (1972).

Table 14. TOXICITY OF CAPTAN: 96-HR TL_{50} AND LTC FOR THREE SPECIES OF FISH[a]

Species	Mean temperature (and range) (°C)	96-Hr TL_{50}[b] (µg/ℓ)	LTC[b,c] (µg/ℓ)
Fathead minnow	25.0 (25.1-25.4)	65 (59-72)	64 (58-70)
Bluegill	25.0 (24.8-25.0)	72 (47-111)	72 (47-111)
Brook trout	11.7 (11.5-12.0)	34 (22-52)	29 (18-46)

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[a] Hermanutz et al., *op. cit.* (1973).

[b] 95% confidence limits in parentheses.

[c] Lethal threshold concentration.

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Table 15. TOXICITY OF CAPTAN TO FISH IN STANDARD RECONSTITUTED STATIC WATER AT 12°C

Formulation	Average weight (g)	Species	LC_{50} Values (µg/ℓ) and 95% confidence limits 24 hr	96 hr
Captan (90-98%)	0.81	Coho salmon	138 118-160	137 117-160
Captan (90-98%)	0.70	Chinook salmon	139 115-168	120 103-140
Captan (90-98%)	0.73	Brown trout	81.0 69.8-94.0	80.0 63.8-100
Captan (90-98%)	0.42	Lake trout	53.0 44.5-63.1	49.0 40.1-59.9
Captan (90-98%)	0.34	Fathead minnow	290 211-398	200 168-238
Captan (90-98%)	0.67	Yellow perch	540 420-695	420 311-520

Data from Mauck, *op. cit.* (1972).

Table 16. TOXICITY OF CAPTAN TO FISH IN CITY FILTERED WATER AT 12°C (FLOW-THROUGH SYSTEM)

Formulation	Average weight (g)	Species	LC_{50} Values (µg/ℓ) and 95% confidence limits 24 hr	96 hr
Captan (90-98%)	0.75	Coho salmon	75.0 65.0-86.6	56.5 52.3-61.0
Captan (90-98%)	0.60	Brown trout	26.2 21.9-31.3	26.2 21.9-31.3
Captan (90-98%)	0.42	Lake trout	75.0 51.7-109	51.0 39.3-66.2
Captan (90-98%)	0.43	Fathead minnow	152 124-186	134 101-178
Captan (90-98%)	1.1	Yellow perch	> 154	123 98.8-153

Data from Mauck, *op. cit.* (1972).

Table 17. SURVIVAL AND GROWTH OF FATHEAD MINNOWS DURING CHRONIC EXPOSURE TESTS

Item	Measured captan concentration (µg/ℓ)											
	63.5		39.5		16.8		7.4		3.3		0 (control)	
	A[a/]	B	A	B	A	B	A	B	A	B	A	B
					51 Days							
Survival (%)	4 b/	0	80	72	84	88	92	84	76	72	88	80
Total length (mm)												
Mean	-	-	21.3 b/	20.2	21.6	22.0	21.6	22.0	23.4	22.1	23.0	22.4
Range	-	-	28-16	30-13	29-14	32-13	34-13	28-13	33-19	31-14	33-10	30-12
					45 Weeks							
Survival (%)	0 b/	0	73.3	80.0	100	92.3	100	100	100	90.9	100	90.9
Males/females at termination	-	-	5/6	6/7	6/5	5/7	6/4	5/6	6/5	3/7	5/8	4/6
Mean total length (mm)												
Male	-	-	57.4 b/	63.7	64.5	67.4	69.2	65.2	61.2	63.3	64.2	69.3
Female	-	-	50.0 b/	51.4	50.6	54.9	55.5	57.0	59.2	54.4	58.1	58.5
Mean weight (g)												
Male	-	-	2.4	3.2	3.2	3.7	4.0	3.2	2.5	3.1	2.8	3.8
Female	-	-	1.3	1.4	1.3	1.5	1.6	1.7	1.7	1.4	1.7	1.8

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a/ A and B indicate duplicate test chambers.
b/ Values are significantly different from controls (P = 0.05).
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Source: Hermanutz et al., *op. cit.* (1973).

Although statistical significance could not be shown, the investigators reported that mean spawnings per female and mean eggs spawned per female appeared to be adversely affected at 39.5 and 16.8 µg/liter. Growth and survival of the F_1 generation were reduced in 39.5 µg/liter after 30 days but no significant differences in growth or survival of the F_1 generation were observed between treatments at 16.8, 7.4, and 3.3 µg/liter and the untreated controls.

The scientific names of the fish studied in this review are listed in Table 18.

Feeble swimming at the surface was reported by Hermanutz et al. (1973) to be a characteristic response in fathead minnows, to exposure to captan.

There is no known data on the effects (if any) of captan to fishes under field conditions, although registered labels of captan-containing commercial pesticides carry the caution statement "This product is toxic to fish. Keep out of lakes, streams or ponds." (Captan is not registered for use directly on bodies of water.)

Lower Aquatic Organisms

Laboratory studies - Frear and Boyd (1967)[1] observed a LC_{50} (26 hr) of 1.3 ppm for Daphnia magna in a static water system.

Paris and Lewis (1973)[2] conducted a comprehensive literature search on the role of aquatic microbial metabolism in the environmental degradation of 10 selected pesticides, including captan. There is little available information in this area to date. The U.S. Environmental Protection Agency's Athens, Georgia, Laboratory, has initiated experimental work on the interactions between captan and aquatic organisms. Various studies on captan began at the end of 1973. In preliminary experiments with captan, the concentration of the fungicide decreased rapidly in bacterial cultures to which it was added. Only traces of the 3.0 ppm initial concentration were still detectable after 19 hr. The concentration of captan decreased more rapidly in the inoculated than in uninoculated preparations.

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[1] Frear, D. E. H., and J. Boyd, "Use of Daphnia magna for microbioassay of Pesticides," J. Econ. Entomol., 60:1228-1236 (1967).

[2] Paris, D. F., and D. L. Lewis, "Chemical and Microbial Degradation of 10 Selected Pesticides in Aquatic Systems," Residue Rev., 45:95-124 (1973).

Table 18. SPECIES OF FISH USED
IN TOXICITY TESTS WITH CAPTAN

Common name	Scientific name
Bluegills	*Lepomis macrochirus*
Brook trout	*Salvelinus fontinalis*
Brown trout	*Salmo trutta*
Carp	*Cyprinus carpio*
Channel catfish	*Ictalurus punctatus*
Chinook salmon	*Oncorhynchus tshawytscha*
Coho salmon	*Oncorhynchus kisutch*
Cutthroat trout	*Salmo clarki*
Fathead minnow	*Pimephales promelas*
Goldfish	*Carassius auratus* (*Cyprinus auratus*)
Lake trout	*Salvelinus namaycush*
Rainbow trout	*Salmo gairdneri*
Yellow perch	*Perca flavescens*
Zebrafish	*Brachydanio rerio*

Lazaroff (1967)[1] studied the effects of pesticides on freshwater algae in order to evaluate the use of such organisms in biological assays for pesticide pollution. In enrichment cultures, algal development was initially inhibited by captan at 1.0 ppm. Eventually, algal growth developed in such preparations due to the selections of resistant forms.

Field studies - Brisou and Denis (1969)[2] also used a bacteriological method to monitor pesticides in seawater, shore mud, and shellfish including oysters, clams, cockles and mussels. In their method, the shellfish are removed from their shells and pulverized mechanically. Pesticide residues were extracted by suitable solvents and the use of appropriate extraction and centrifugation equipment and procedures. Bands of heavy blotting paper are impregnated with the final extracts, dried, and then placed on a nutrient medium in a petri dish with strains of *Bacillus licheniformis* and *Flavobacterium* sp. These cultures are then incubated for 20 to 24 hr at 37°C. A zone of growth inhibition around the paper bands characterizes a positive result. In this procedure, captan demonstrated "very great inhibitory activity" for both test organisms. The authors state that the method is specific for captan and carbamates.

No additional reports on the interactions between captan and lower aquatic organisms were found. The data reviewed in this area is not sufficient for making an evaluation of captan's effects on aquatic microorganisms. No data were obtained on possible effects of captan on phytoplankton or most other aquatic plants, zooplankton, or benthic invertebrates. The summary of data on the toxicity of pesticides to aquatic animals in the Federal Water Pollution Control Administration's Publication on "Water Quality Criteria" does not include any data on captan. The review of the ecological effects of pesticides on nontarget species by Pimentel (1971)[1] likewise does not contain any information on the effects of captan on aquatic organisms.

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[1] Lazaroff, N., "Algal Response to Pesticide Pollutants," *Bacteriol. Proc.*, 48 (1967).

[2] Brisou, J., and F. Denis, "The Use of Bacteria for the Detection of Certain Pesticides," *Compt. Rend. Soc. Biol.*, 163(6):1426-1427 (1969).

[3] Pimentel, D., "Ecological Effects of Pesticides on Nontarget Species," Executive Office of the President, Office of Science and Technology, Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. (1971).

Effects on Wildlife

Laboratory Studies - Heath et al. (1972)[1] have calculated LC_{50} values (ppm in feed) for four species of birds. The values were determined by administering captan to mallards, pheasants, bobwhite quail and Japanese quail for 5 days; test animals were 2 weeks of age. The data from these determinations are summarized as follows:

Specie	Number of concentrations tested	Birds per concentration	LC_{50} (ppm in feed)
Bobwhite quail	6	8	> 2,400
Japanese quail	3	14	> 5,000
Pheasant	3	12	> 5,000
Mallard duck	3	10	> 5,000

Schafer (1972)[2] found captan not to be toxic to the red-winged blackbird (Agelaius phoeniceus) or the starling (Sturmus vulgaris) at a single oral dose of 100 mg/kg.

Based on these limited data, the toxicity of captan to birds does not appear to be of a high order by dietary routes. Dermal toxicity, inhalation toxicity, etc., have not been reported.

No reports were found on toxicity of captan to wild mammals as determined by controlled studies.

Field Studies - Data on the effects (if any) of captan to wildlife under field conditions appear to be nonexistent.

Data from laboratory investigations on the toxicity of captan to birds indicate that captan is relatively nontoxic to these species. As far as could be determined, no adverse effects on wildlife have been attributed to captan in more than 20 years of commercial use in the U.S. and in many other countries.

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[1] Heath, R. G., J. W. Spann, E. F. Hill, J. F. Kreitzer, "Comparative Dietary Toxicities of Pesticides to Birds," U.S. Bureau of Sport Fisheries and Wildlife, Special Scientific Report, Wildlife No. 152, pp. 1-40 (1972).

[2] Schafer, E. W., "The Acute Oral Toxicity of 369 Pesticidal Pharmaceutical, and Other Chemicals to Wild Birds," Toxicology and Applied Pharmacology, 21, 315-330, (1972).

Effects on Beneficial Insects

Bees - Beran and Neururer (1955)[1] investigated the toxicity to bees of a large number of pesticides, including captan. The LD_{50} of captan, when fed orally, was 2.44 µg/bee, placing it among those pesticides considered to be relatively nontoxic to the honeybee.

Anderson et al. (1957)[2] found no significant mortality associated with bees sprayed with captan at two pounds/100 gal.

Parasites and Predators - Bartlett (1963)[3] reported that when captan was sprayed in orchards at the rate of 1 lb/100 gal. of water some mortality of parasitic wasps (especially *Metaphycus helvolus*) occurred. There was little or no mortality of predatory coccinellid beetles.

Croft and Nelson (1972)[4] studied the toxicity of more than 20 commonly used pesticides including captan to several populations of the beneficial predatory mite *Amblyseius fallacis*. Predators were collected in August and September from several commercial Michigan apple orchards, and laboratory colonies started. Toxicity was determined by exposing mites to slides, and, in another test series, to apple leaf disks immersed in field use concentrations of the test pesticides. By both methods, captan had little activity on several strains of *A. fallacis*.

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[1] Beran, F., and J. Neururer, "The Action of Plant Protectants on the Honey Bee (*Apis mellifera*). I. Toxicity of Plant Protectants to Bees," *Pflanzenschutz Ber.*, 15:97-147 (1955).

[2] Anderson, E. J., F. R. Shaw, and D. J. Sutherland, "The Effects of Certain Fungicides on Honey Bees," *Jour. Econ. Ento.*, 50(6), 570-573, (1957).

[3] Bartlett, B. R., "The Contact Toxicity of Some Pesticide Residues to Hymenopterous Parasites and Coccinellid Predators," *J. Econ. Entomol.*, 56:694-698 (1963).

[4] Croft, B. A., and E. E. Nelson, "Toxicity of Apple Orchard Pesticides to Michigan Populations of *Amblyseius fallacis*," *Environ. Entomol.*, 1(5):476-579 (October 1972).

Nelson et al. (1973)[1] studied the toxicity of pesticides including captan to another important predatory mite Agistemus fleschneri. Field collected specimens were exposed to the test pesticides in the laboratory by the slide-dip method. Slides treated with captan at the rate of 2 lb AI/100 gal. of a 50% wettable powder formulation produced the lowest percent mortality (1.3% at 48 hr) among 35 pesticides studied. In field tests, five applications of captan 50% wettable powder (three at 20 ounces, two at 10 ounces/100 gal.) were not toxic to the predatory mite, nor to the phytophagous mite Panonychus ulmi. In mixtures with insecticides, the presence of captan in the combination did not result in higher predator mortality. The authors characterize captan as "rather innocuous" to A. fleschneri.

Several Canadian and European workers report generally similar observations. MacPhee and Sanford (1956[2] and 1971[3]) studied the influence of spray programs on the fauna of apple orchards, specifically beneficial arthropods. Captan was found to be "relatively harmless." There was little or no reduction in the number of beneficial predacious and parasitic arthropods when captan was used in orchards at recommended rates.

Benoit and Parent (1973)[4] studied the population densities of the European red mite (Panonychus ulmi), on apples in Quebec during the period 1960 through 1967. Abiotic factors responsible for the natural reduction of P. ulmi were predacious mites, arachnids, coccinellids, pentatomids, thrips and mirids. The experimental plot where these studies were conducted was sprayed regularly with fungicides, primarily captan, for the control of diseases. The captan sprays did not appear to adversely affect any of the natural enemies of the European red mite.

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[1] Nelson, E. E., B. A. Croft, A. J. Howitt, and A. L. Jones, "Toxicity of Apple Orchard Pesticides to Agistemus fleschneri," Environ. Entomol., 2(2):219-222 (1973).

[2] MacPhee, A. W., and K. H. Sanford, "Influence of Spray Programs on the Fauna of Apple Orchards in Nova Scotia. X. Effects of Some Beneficial Arthropods," Can. Entomol., 88:631-634 (1956).

[3] MacPhee, A. W., and K. H. Sanford, "The Influence of Spray Programs on the Fauna of Apple Orchards in Nova Scotia. XII. Second Supplement to VII. Effect on Beneficial Arthropods," Can. Entomol., 93:671-673 (1961). In: Pimentel (1971).

[4] Benoit, J. P. H., and B. Parent, "Natural Population Densities of the European Red Mite on Apple in Quebec," Environ. Entomol., 2(6):1064-1068 (1973).

Schneider (1958)[1] found that captan at normal rates of application in orchards had no effect on the parasitic wasp, *Aphelinus mali*. Van deVrie (1967),[2] however, found that when captan was applied to apple trees at the rate of 0.15%, some mortality to *Aphelinus mali*, and also to the predatory bug *Orius* sp. resulted. In the same study, Van deVrie found this rate of captan to be harmless to the predatory bug, *Anthocoris nemorum*.

Besemer (1964)[3] found that captan applied to fruit trees at normal recommended dosages did not harm the beneficial predatory mite, *Thyplodromus* sp., or such beneficial parasitic wasps as *Mormoniella* sp. and *Aphelinus mali*.

Ankersmit et al. (1962)[4] reported that in laboratory tests, a spray concentration of captan of 0.125% caused no mortality to the parasitic wasp, *Mormoniella vitripennis*.

In tests of potted apple trees, captan at the rate of 0.2% caused little or no toxicity to beneficial predatory mites (Van deVrie, 1962[5]).

Ulrich (1968)[6] found that captan residues remaining on a surface after treatment at the rate of 1,000 ppm had little or no effects on female adults of the parasitic wasp *Trichogramma* sp. when exposed for 10 hr.

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[1] Schneider, H., "Untersuchungen uber den Einfluss neuzeitlicher Insektizide und Fungizide auf die Blutlauszehrwesp (*Aphelinus mali* Hald.)," *Z. Ang. Ent.*, 43:173-196 (1958). In: Pimentel (1971).

[2] Van deVrie, M., "The Effect of Some Pesticides on the Predatory Bugs *Anthocoris nemorum L.* and *Orius* Spec. and on the Wooly Aphid Parasite *Aphelinus mali* Hald.," *Entomophaga*, Me. hors Serie 3:95-101 (1967). In: Pimentel (1971).

[3] Besemer, A. F. H., "The Available Data on the Effect of Spray Chemicals on Useful Arthropods in Orchards," *Entomophaga*, 9:263-269 (1964). In: Pimentel (1971)

[4] Ankersmit, G. W., J. T. Locher, H. H. W. Velthuis, and K. W. B. Zwart, "Effect of Insecticides, Acaricides, and Fungicides on *Mormoniella vitripennis* Walker," *Entomophaga*, 4:251-255 (1962). In: Pimentel (1971).

[5] Van deVrie, M., "The Influence of Spray Chemicals on Predatory and Phytophagous Mites on Apple Trees in Laboratory and Field Trials in the Netherlands," *Entomophaga*, 7:243-250 (1962). In: Pimentel (1971).

[6] Ulrich, H., "Versuche uber die Empfindlichkeit von *Trichogramma* (*Hymenoptera*, Chalcidoidea)gegenuber Fungiziden," *Anz. Schadlingskunde*, 51:101-106 (1968). In: Pimentel (1971).

Russian workers (Kapitan et al., 1972[1]) investigated the toxicity of a number of pesticides to larvae of the aphid lion, Chrysopa carnea. The pesticides were applied at concentrations ranging from 0.03 to 1.0%. Captan was among those least toxic to this predator.

These observations by U.S., Canadian, West European, and Russian workers indicate that captan at fungicidally effective rates of application appears to be relatively harmless to beneficial predators and parasites occurring in deciduous fruit orchards. Among all of the accounts reviewed above, there was only one report of "some mortality" to the predatory bug Orius sp., and to the parasitic wasp, Aphelinus mali.

Interactions with Lower Terrestrial Organisms

Microflora - Agnihotri (1971)[2] studied the persistence of captan and its effects on the microflora, respiration and nitrification of a forest nursery soil. Captan was applied to the soil (fine sand with 3.8% organic matter and a pH of 6.1) at the rates of 62.5, 125 and 250 ppm. Ammonium sulfate (100 ppm N) was thoroughly mixed with the soil, and calcium carbonate was added to neutralize the acidity produced in nitrification. The soil moisture was adjusted, and the soil samples thus prepared were incubated in the laboratory in glass pint milk bottles. Captan affected the soil microflora and some of its activities. Captan killed the population of two pathogenic fungi, Rhizoctonia and Pythium spp. After an initial decrease, the population of actinomycetes increased gradually. Some bacteria also increased, but after 35 days, the population had dropped back to that of the control soil. All concentrations of captan tested impaired nitrification for varying periods of time. Respiration in the soil was inhibited initially, but was subsequently stimulated. The author suggests that this may have been due to the use of captan decomposition products by the microorganisms. The initial depression of carbon dioxide production was directly proportional to the captan concentration in the soil.

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[1] Kapitan, A. I., G. I. Sukhoruchenko, and Y. S. Tolstova, "Toxicity of Pesticides for Aphid Lions," Zashch. Rast., 7:24-25 (Moscow) (1972).

[2] Agnihotri, V. P., "Persistence of Captan and Its Effects on Microflora, Respiration and Nitrification of a Forest Nursery Soil," Can. J. Microbiol., 17(3):377-383 (1971).

Wainwright and Pugh (1973)[1] investigated the effects of captan on the nitrification rate of soil amended with ammonium sulfate in comparison to soils not treated with a fungicide, but also amended with ammonium sulfate. Under these conditions, low concentrations of captan (5 µg AI/g of soil) stimulated nitrification activity of the soil, while ammonification was not significantly affected. However, at (unspecified) higher concentrations, ammonification appeared to be markedly increased. It is noted that the rate of 5 µg of captan per gram of soil which stimulated nitrifiction in these tests is more than 10 times lower than the lowest rate studied by Agnihotri (1971).

Chinn (1973)[2] studied the effects of captan (and several other fungicides) on microbial activities in the soil by a bioassay method. Included in these tests were three species of bacteria, two of actinomycetes, and three of fungi. Captan (and two other fungicides) showed little or no activity under these conditions. Concentrations studied ranged from 1.0 to 1,000 ppm. The author points out that the captan results may have been influenced by its low solubility.

Tews (1971)[3] investigated the effects of captan and a number of other fungicides on the microfungi of a cattail marsh. Captan at "field concentration" was applied to cultures of the predominant microfungi of the marsh, i.e., _Hansenula saturnus_, _Mucor hiemalis_, _Penicillium stipitatum_, and _Trichoderma viride_. The growth of all four fungi was inhibited by captan. However, when captan was subsequently applied to field plots in a cattail marsh, it did not reduce the number of microfungal propagules in the litter, water or mud, while several other chemicals studied did produce such effects. This study was unreplicated and preliminary in nature.

Hansen (1972)[4] studied the effects of captan and other fungicides on 211 strains of bacteria isolated from various soils, from marine and freshwater sediments, and from outdoor dust. Several of the chemicals tested produced a marked inhibitory effect, and there were considerable differences between chemicals and test organisms. The author concluded that captan appears to pose no risk to a bacterial population since most strains were "resistant or relatively resistant" to it.

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[1] Wainwright, M., and G. J. F. Pugh, _Soil Biol. Biochem._, 5(5):577-584 (1973).

[2] Chinn, S. H. F., "Effect of Eight Fungicides on Microbial Activities in Soil as Measured by a Bioassay Method," _Can. J. Microbiol._, 19(7): 771-777 (1973).

[3] Tews, L. L., "Effects of Selected Fungicides and Soil Fumigants Upon the Microfungi of a Cattail Marsh," _Proc. Conf. Great Lakes Res._ (14th), pp. 128-136 (1971).

[4] Hansen, J. C., "The Effect of Some Sulphur and Mercury Containing Fungicides on Bacteria," _Chemosphere_, 1(4):159-162 (1972).

Naumann (1970)[1] studied the effects of captan and several other fungicides on the soil microflora. In field and greenhouse trials, captan at the concentration of 250 ppm stimulated the soil bacteria in loam soil for about 12 weeks. Actinomycetes were least affected. Most of the physiological groups of the soil bacteria such as nitrogen-fixing organisms, cellulose decomposers, spore-forming bacteria, and denitrifying bacteria were stimulated. In some instances, the addition of captan resulted in a decrease in the nitrifying bacteria, ammonifying forms, anaerobic bacteria, and soil algae. Azotobacter chroococcum was significantly inhibited for several weeks. Many soil fungi including Penicillium, Aspergillus, Trichoderma, Cephalosporium, Hyalopus, Acrostalagmus, Verticillium, Aleurisma, Sporotrichum, Strachybotrys, Phymatotrichum, Phoma, Spicaria, Hormodendrum, Claddsporium, Scopulariopsis, Oospora and Fusarium were reduced markedly by the application of captan. After a short inhibition, the soil respiration was stimulated by 250 ppm of captan, while the dehydrogenase activity was strongly reduced for 4 weeks.

Domsch (1959)[2] reported that the effect of captan on the soil microflora varies with the dosage rates. Applied to soil at the "low" rate of 400 to 600 ppm, captan reduced the populations of sensitive algae, actinomycetes and fungi, while bacterial numbers remained unchanged. Picci (1956)[3] found that at the rate of 1,000 ppm, captan inhibited nitrifying bacteria, but affected ammonifying bacteria only slightly. Both Picci (1956) and Domsch (1959) observed that little permanent damage occurs to fungi such as Penicillium, Pythium, Fusarium, and Rhizoctonia in soils treated with captan. Lukens (1968)[4] found Trichoderma to be quite resistant to captan also. Torgeson (1969)[1] states that "soil bacteria are resistant to captan."

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[1] Naumann, K., Jr., "The Dynamics of Soil Microflora After the Use of the Fungicides Olpisan (Trichlorodinitrobenzene), Captan and Thiuram," Arch. Pflanzenschutz, 6(5):383-398 (1970).

[2] Domsch, K. H., "The Effects of Soil Fungicides. III. Quantitative Changes in Soil Flora," Z. Pflanzenkrankh. Pflanzenschutz, 66:17-26 (1959).

[3] Picci, G., "Effect of Captan on Soil Microorganisms," Agr. Ital. (Pisa) 56:376-382 (1956). In: Torgeson (1969).

[4] Lukens, R. J., (1968), unpublished data, quoted from Torgeson, D.C. (1969).

Kokke (1970)[2] studied the soil and water microflora in search of DDT-accumulating, resistant, sensitive, and degrading microorganisms. Microbial cultures were isolated from tap water, polluted surface water, garden soil, and recently pesticide treated nursery soil. The author reports that DDT-accumulating bacteria were more plentiful in the media on which captan had been sprayed.

Langkramer (1970)[3] applied a "rapid and simple" laboratory method for testing the effects of captan and other pesticides on soil biota. This German paper, available to us only in abstract form, includes a fairly detailed description of the method, but no results.

Tiefenbrunner (1973)[4] reported that captan decreased the formation of aerobic mycelia in cultures of _Suillus plorans_ when added to culture media at 0.05, 0.1, and 0.3%.

Several authors investigated the effects of captan on beneficial soil microorganisms, particularly the nitrogen-fixing bacteria of leguminous plants.

Gillberg (1971)[5] studied the effects of captan on two strains each of _Rhizobium meliloti_, _R. leguminosarum_, and _R. trifolii_. These organisms were plated on a glucose medium containing various concentrations of captan. Resistant mutants were selected by culturing techniques and ultraviolet irradiation was used to induce mutations when no spontaneous mutants were found. All wild strains were inhibited by captan at 50 µg/ml. Spontaneous mutants resistant to this captan concentration were isolated from all but one of the strains. The ability to infect leguminous plants was not affected in any of the resistant mutants that were isolated.

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[1] Torgeson, D. C. (ed.), "Fungicides, an Advanced Treatise," Vol. II. "Chemistry and Physiology," Chapter V., "Captan and the R-SCCl$_3$ Compounds," Academic Press (1969).

[2] Kokke, R., "DDT: Its Action and Degradation in Bacterial Populations," _Nature_, 226(5249):977-978 (1970).

[3] Langkramer, O., Jr., "Investigations Into the Influence of Pesticides on Soil Microorganisms in Pure Cultures by Means of a Laboratory Method," _Zentr. Bakteriol. Parasitenk._, Abt. II.: Na; 125(7):713-722 (1970).

[4] Tiefenbrunner, F., "Mycelial Weight Increase of Myconnhizal Fungi Under the Influence of Fungicides _in vitro_," _Z. Pilzk._ 38(1-4): 105-107 (1973).

[5] Gillberg, B. O., "On the Effects of Some Pesticides on _Rhizobium_ and Isolation of Pesticide-Resistant Mutants," _Arch. Mikrobiol._, 75(3): 203-208 (1971).

Petrovic (1970)[1] studied the effect of several pesticides on the nodulation of alfalfa and red clover. Captan (concentration not given) was more toxic to the nodulation of alfalfa than of red clover, while the reverse was true for another fungicide studied under the same conditions.

Mukewar and Bhide (1969)[2] and Muthusamy (1973)[3] studied the effects of captan on the nodulation of peanuts (groundnuts) by Rhizobium species. Mukewar and Bhide found no significant effects on nodule numbers or plant weight with peanut seeds grown on steamed soil treated with captan (rate not given). When peanuts were grown on unsterilized soil fungicide treatment increased both the nodule number and plant weight. When Rhizobium inoculated plants were grown in sterilized soil, sterilized sand, or unsterilized soil from captan treated seeds, higher plant weight and nodule numbers were observed in comparison to uninoculated controls not treated with the fungicide. The authors conclude that treatment of peanut seeds with captan as a seed protectant will not adversely affected bacterial inoculants. By contrast, Muthusamy (1973) reported that seed treatment of peanuts with captan at the rate of 2 g/kg of seed inhibited Rhizobium growth. The reasons for these divergent observations are not clear from the available data.

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[1] Petrovic, V., "Effect of Some Pesticides on Nodulation of Medicago sativa (Alfalfa) and Trifolium pratense (Red Clover)," Mikrobiologija, 7(2):183-193 (1970).

[2] Mukewar, P. M., and V. Bhide, "Effect of Seed Treatment with Fungicides and Antibiotic Aureofungin on Nodulation by Rhizobium in Groundnut," Hindustan Antibiot. Bull., 12(2-3):75-80 (1969).

[3] Muthusamy, S., "Effect of Seed Dressing and Soil Fungicides on the Growth of Rhizobium in Groundnut," Pesticides, 7(1):27-28 (1973).

Fiscor and Nii Lo Piccolo (1970)[1] studied the effects of temperature on the mutagenicity of captan to several strains of E. coli and S. typhimurium using captan in the form of "tomato vegetable dust" (concentration not given in abstract). A 1:10 suspension of the pesticide in sterile distilled water was prepared, and aliquots were allowed to stand at room temperature, steamed-sterilized for 15 min at about 100°C, and autoclaved for 15 min at 15 lb pressure at about 121°C, respectively. After cooling, these captan-containing suspensions were placed on plate cultures of the test organisms. Mutagenic response was determined by counting the number of revertant colonies appearing on the plates in 96 hr at 37°C. All captan treatments significantly increased reversions compared to the controls. The steam-sterilized pesticide induced five times fewer reversions, the autoclaved material 21 times fewer reversions than the room temperature check.

Microfauna - Drift (1970)[2] reviewed the interrelationships between a number of pesticides and the soil fauna. Captan had only a temporary effect on the microfauna including millipedes, dipterous larvae, collembola, oribatid mites, earthworms, enchytraeids, nematodes, insect larvae, centipedes, mesostigmatic mites, carabids and spiders. Soils studied included samples of arable land, horticultural soils, grassland, orchards, and woodlands.

Martin and Wiggans (1959)[3] studied the toxicity of captan to earthworms, Eisenia foetida, in the laboratory. When earthworms were immersed for 2 hr in suspensions of captan at 10 ppm, there was little mortality, but at 100 ppm all of the earthworms were killed.

DeVries (1962)[4] investigated the toxicity of moderate and very high rates of captan to two species of earthworms. Soil treated with captan at 15, 60 and 500 lb/acre was nontoxic to Lumbricus species after 32 days exposure. *Helodricus* species was unaffected at the two lower rates, but there was 47% mortality after 32 days exposure to the 500 lb/acre rate.

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[1] Fiscor, G., and G. M. Nii Lo Piccolo, "The Effect of Temperature on the Mutagenicity of Captan," Newslett. Environ. Mutagen Soc., 3:38 (1970).

[2] Drift, J., "Pesticides and Soil Fauna," Meded. Rijksfac. Landbouwwetensch Gent, 35(2):707-716 (1970).

[3] Martin, W. L., and S. C. Wiggans, "The Tolerance of Earthworms to Certain Insecticides, Herbicides, and Fertilizers," Oklahoma Agr. Exp. Stat. Proc. Ser. P-334 (1959). In: Pimentel (1971).

[4] DeVries, M. L., "Effect of Biocides on Biological and Chemical Factors of Soil Fertility," Ph.D. Dissertation, University of Wisconsin, Madison, Wisconsin, 89 pages (1962). In: Pimentel (1971).

The data reviewed in this subsection indicate that captan affects a number of soil bacteria and fungi under laboratory conditions. Under field conditions, effects from normal concentrations (i.e., those resulting from application at recommended rates) of captan appear to be either nonexistent or very short-lived. In addition to its principal use as a foliar fungicide, captan is recommended as a seed protectant, as a dip for the control of rots and damping off of cuttings and bulbs, as a potato seed piece treatment for the control of rots, and for the control of some diseases on turf and lawns. Some recommendations on some labels also provide for broadcast application directly into the soil, but these uses are very minor. Thus, the use of captan in accordance with the registered labels will generally not result in high captan concentrations in the soil.

Few reports were found on the toxicity of captan to the lower terrestrial fauna. Hewever, the review by Drift (1970) and the reports on earthworms indicate that captan is relatively nontoxic to such organisms.

Residues in Soil

Laboratory and Field Studies - Munnecke (1958)[1] studied the soil persistence of captan and three other nonvolatile diffusible fungicides in a soil mix containing by volume 50% fine sand and 50% Germam peat moss. Twenty milliliters of a suspension containing 1,000 ppm of captan active ingredient (AI) were added to flasks containing 30 g of this soil mixture, plus a full complement of fertilizers. Prior to addition of the fungicide, the flasks were treated in three different ways: one lot was sterilized for 1 hr at 10 to 12 lb psi steam pressure; one lot was sterilized with gaseous propylene oxide; and one lot was left untreated. When soil samples were plated, no growth occurred from soil treated with steam or propylene oxide, whereas about 1 million fungal colonies and 2 to 3 million bacterial colonies were produced per gram of untreated soil. The fungicides were added after these steps. The fungicidal activity in the soils was determined at intervals for up to 150 days by a bioassay technique using agar plates seeded with spores of *Myrothecium verrucaria*. Under these conditions, the activity of captan persisted for at least 65 days. There were no significant differences between untreated, steamed, or propylene oxide-treated soil.

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[1] Munnecke, D. E., "The Persistence of Nonvolatile Diffusible Fungicides in Soil," *Phytopathology*, 48:581-585 (1958).

Burchfield (1959)[1] investigated the stability of captan and three other fungicides in a silt loam soil with a natural pH of 4.5 to 5. This soil was composted with manure and fertilizer, and with sufficient limestone to increase the pH to above 6, then stored in the field for 2 to 3 years. Captan was mixed at rates of 10 and 100 µg of active ingredient per gram of soil with moist and air dried soil. The moist soil had a pH of 6.4 and contained 17.5% water; the air dried soil had a pH of 6.2 and contained 1.6% water. Captan residues remaining in the soil samples were analyzed colometrically. The half-life of captan in the dry soil was more than 50 days; in the moist soil, 3.5 days; and in a phosphate buffer (pH 7), 0.1 day.

Kluge (1969)[2] studied the effects of soil pH on the degradation and residual effectiveness of captan and two other fungicides in the soil. The rate of degradation of captan was not affected by hydrogen ion concentrations ranging from pH 3.6 to 7.4, while the other two fungicides, TMTD and ferbam, were markedly affected by differences in pH. Captan was applied to the soil in the form of a 50% formulation, at the rate of 200 ppm of active ingredient. Its biological effectiveness declined to less than 10% within 10 weeks after initiation of the test, as determined by a bioassay technique measuring growth inhibition of a test fungus, Rhizoctonia solani, on agar plates.

Griffith and Matthews (1969)[3] investigated the persistence of captan well incorporated into the soil, and added to the soil on the surface of glass beads (simulating seeds). In the first test series, captan at 125 ppm was thoroughly mixed into unsterilized medium loam soil having a moisture content of 45%. In the second series, the fungicide was added to the soil on the surface of 0.7 mm diameter glass beads at a rate equivalent to 125 ppm. The amount of captan remaining in the soil was measured by bioassay after 0, 1, 2, 4, 8, and 21 days. Plugs of soil containing captan were incubated on agar plates seeded with spores of Myrothecium verrucaria, and the diameter of the zone of fungal inhibition was measured. The diameters of the inhibition zones were then converted into parts per million of fungicide by means of regression equations for the calibrations. When mixed with the soil, captan showed very low persistence, having a half-life of 1 to 2 days. By contrast, when added to the soil on the surface of glass beads, captan persisted; there was little change in the initial concentration after 21 days. The authors concluded that captan persists far longer in the soil when localized in high concentrations than when uniformly distributed. The results help to explain the effectiveness of captan as a seed protectant, despite its apparently low persistence in the soil.

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[1] Burchfield, H. P., "Comparative Stabilities of Dyrene, 1-Fluoro-2,4-dinitrobenzene, Dichlone and Captan in a Silt Loam Soil," Contrib. Boyce Thompson Inst., 20:205-215 (1959).

[2] Kluge, E., "Der Einfluss der Bondenreaktion auf den Abbau and die Wirkungsdauer von Thiuram, Ferbam, und Captan in Boden," Arch. Pflanzenschutz, 5(4):263-271 (1969).

[3] Griffith, R. L., and S. Matthews, "The Persistence in Soil of the Fungicidal Seed Dressing Captan and Thiuram," Ann. Appl. Biol., 64(1):113-118 (1969).

Foschi et al. (1970)[1] studied the degradation and vertical movement of captan and several other pesticides in soils. In their tests, DDT, dieldrin, captan and benlate had about the same degree of persistence; another group of pesticides was less persistent.

Suzuki and Nose (1970)[2] studied the decomposition of pentachlorophenol (PCP) in farm soil. At low concentrations (100 ppm), the rate of PCP decomposition varied with soils, but at high concentrations (1,000 ppm) there were few differences in the rate of PCP decomposition between different soil types at 20 and 28°C. The rate of PCP decomposition was suppressed slightly when captan was added to the system.

Pack (1974)[3] studied the fate of 5.33 ppm of ^{14}C carbonyl-labeled captan in a sandy loam soil. Degradation was rapid; after 7 days 99% of the captan had been degraded. Other than $^{14}CO_2$, the two major metabolites were tetrahydropthalimide, which reached a maximum level of 66% of applied ^{14}C in 7 days, and tetrahydropthalimic acid which reached a maximum level of 16.5 per cent in 14 days. Several other minor products were observed, but all reached a maximum level within 37 days. $^{14}CO_2$ evolution was measured throughout the experiment; after 322 days 95% of the applied radioactivity could be accounted for as $^{14}CO_2$.

Monitoring Studies - Stevens et al. (1970)[4] reported on a pilot monitoring study conducted nationwide at 51 locations in 1965, 1966, and 1967 to determine pesticide residue levels in soil. Samples were collected from 17 areas in which pesticides were used regularly, 16 areas with a record of at least one pesticide application, and 18 areas with no history of pesticide use. Pesticide use records indicating that captan had been used at a number of the sites samples, including Dade County, Florida; Adams County, Pennsylvania; Quincy-Moses Lake, Washington; and Tulelake, California; and in other fruit growing areas. However, no detections of captan residues were reported.

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[1] Foschi, S., Jr., A. Cesari, Jr., I. Ponti, Jr., P. G. Bentivogli, Jr., and A. Bencivelli, Jr., "Study of the Degradation and Vertical Movement of Pesticides in Soil," Notiz. Mal. Piante, 82(3):37-49 (1970).

[2] Suzuk-, T., Jr., and K. Nose, Jr., "Decomposition of Pentachlorophenol in Farm Soil. I. Some Factors Relating to PCP Decomposition," Noyaku Seisan Gijutsu, 22:27-30 (1970).

[3] Pack, D. E., "The Soil Metabolism of Carbonyl ^{14}C-Captan," Chevron Chemical Co., San Francisco, Calif., File No. 773.21 (October 23, 1974).

[4] Stevens, L. J., C. W. Collier, and D. W. Woodham, "Monitoring Pesticides in Soils from Areas of Regular, Limited, and No Pesticide Use," Pest. Monit. J., 43(3):145-163 (1970).

In the National Soils Monitoring Program for pesticides, 1,729 samples of cropland soils from 43 states were collected in 1969 (Wiersma et al., 1972[1]). Pesticide use records indicated that captan had been used at 11.16% of 1,684 sites sampled, at an average application rate of 0.12 lb AI/acre. No detections of any captan residues were reported.

In the National Soils Monitoring Program for pesticides in 1970 (Crockett et al., 1970[2]), soil and crop samples were collected from 1,506 cropland sites in 35 states. Pesticide use records indicated that captan was used at 106 (7.88%) of the 1,346 sites sampled, at mean application rate of 1.68 lb AI/acre. Crops receiving captan applications included field corn, cotton, and soybeans. Again, there are no reports of any captan residues detected.

Carey et al. (1973)[3] monitored organochlorine pesticide residues in soils and crops of the corn belt region in 1970. Samples of soil, corn, cornstalks, soybeans, sorghum grain, sorghum fodder, and mixed hay were obtained from 400 sites in 12 corn belt states. Pesticide use records indicated that captan had been used at 68 of the 400 sites sampled, at an average application rate of 0.03 lb AI/acre. Captan was the second most widely used pesticide, after atrazine. The residue analysis method employed was capable of detecting captan. No captan residues were detected in any of the soil, plant or seed samples analyzed.

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[1] Wiersma, G. B., H. Tai, and P. F. Sand, "Pesticide Residue Levels in Soils, FY 1969-National Soils Monitoring Program," Pest. Monit. J., 6(3):194-201 (1972).

[2] Crockett, A. B., G. B. Wiersma, H. Tai, W. G. Mitchell, and P. J. Sand, "National Soils Monitoring Program for Pesticide Residues - FY 1970," U.S. Environmental Protection Agency, Technical Services Division (unpublished manuscript) (1970).

[3] Carey, A. E., G. B. Wiersma, H. Tai, and W. G. Mitchell, "Organochlorine Pesticide Residues in Soils and Crops of the Corn Belt Region, United States - 1970," Pest. Monit. J., 6(4):369-376 (1973).

The data on captan soil residues reported in the foregoing four reports from the National Soils Monitoring Program for pesticides are subject to question because in this program, soil samples are being shipped and stored at room temperature until processed for analysis, as reported by Stevens et al. (1970). No information is given in these reports on the relationships between time of pesticide application, time of sampling, and time of processing and analysis of the samples. No information is available on the effects of shipping and storage of the samples on the captan residues that may have been present at the time of sampling.

Since the results of the 1972 National Soils Monitoring Program were not yet published at the time of this review, data from this source could not be included.

The scientific data on the residues of captan in the soil reviewed indicate that captan appears to be rapidly degraded in natural soil. Captan is believed to be degradable by biological as well as by chemical mechanisms. When captan is uniformly distributed in the soil, its half-life is about 1 to 2 weeks at the most, only 1 to 2 days in many instances. When applied to the soil at higher concentrations in specific areas (e.g., seed protectant use), captan residues persist longer in those specific locales.

Bioaccumulation, Biomagnification

The propensity of captan for bioaccumulation and biomagnification was recently studies by investigators in Illinois (Illinois Natural History Survey, 1973[1/]), using a laboratory terrestrial-aquatic model ecosystem developed by Metcalf et al. (1971).[2/] The model ecosystem, consisting of a terrestrial-aquatic interface and a seven-element food chain, simulates the application of pesticides to crop plants and the eventual contamination of the aquatic environment. The procedure and results are described below.

[1/] Illinois Natural History Survey, "The Fate of Select Pesticides in the Equatic Environment," unpublished report prepared for the Water Quality Office, Environmental Protection Agency, EPA Grant R-800736, 84 pages (1973).

[2/] Metcalf, R. L., G. K. Sangha, and I. P. Kapoor, "Model Ecosystem for the evaluation of Pesticide Biodegradability and Ecological Magnification," Environmental Science and Technology, 5(8):709-713 (1971).

Sorghum (Sorghum halepense) was grown in sand to a height of 10 to 12 cm, then treated with 5 mg of radiolabeled captan dissolved in acetone. The design of this system and the treatment level correspond to a farm pond surrounded by a watershed under cultivation treated with captan at 1 lb AI/acre. After treatment of the sorghum, larvae of the saltmarsh caterpiller (Estigmene acrea), were added to eat the treated plant, simulating both the first member of a food chain, as well as acting as an effective distributing agent for the labeled pesticide inside the system. The water phase contained several members of a freshwater aquatic food chain, i.e., snails (Physa sp.), water fleas (Daphnia magna), and green filamentous algae (Oedogonium cardiacum). After 27 days, mosquito larvae were added to the system, and after three more days, mosquitofish (Gambusia affinis) were added. At the end of 33 days, the entire system was taken apart, and the organisms and the water extracted and analyzed for radioactivity. In addition, extracts were spotted on thin-layer chromatographic plates, developed with appropriate solvents, and exposed to X-ray film to locate and identify the chemical composition of the compounds in the solvent extract. Metabolites were identified by co-chromatography with hypothesized metabolites, as well as by infrared, nuclear magnetic resonance, and mass spectrometry techniques.

At the end of the 33-day test period, none of the organisms contained any captan residues. In view of the alkaline pH of the aqueous portion of the system, the authors suggest that captan underwent hydrolysis as soon as it came in contact with the water. Small amounts of unidentifiable residues (but no captan) were detected in snails, fish, and algae.

The authors conclude that captan does not persist in water, and that "it appears that continued use of captan will not have any serious environmental impact as it does not persist in the water of this 33-day model ecosystem, nor does it accumulate in the fish which is the upper member of the food chain. The probable reason for the nonpersistence of this fungicide in this model ecosystem is the extremely labile trichloromethyl sulfur-nitrogen bond which can be split either by hydrolysis or reaction with mercaptan groups in biological systems."

Environmental Transport Mechanisms

The data reviewed in the preceding subsections of this report section indicate that under field conditions, captan is relatively rapidly degraded by chemical as well as by biological mechanisms. The degradation of captan in the soil is believed due to chemical hydrolysis and the actions of soil microorganisms. No data was found on whether or not volatilization may be an important environmental transport mechanism for captan. The chemical has a relatively low vapor pressure.

Freed et al. (unpublished data, quoted in von Rumker and Horay, 1972[1/]) determined the propensity of captan for volatilization and leaching under simulated field conditions from loam soils at 25°C at an annual rainfall of 59 in. Volatilization of pesticides under these conditions, i.e., from a porous, sorptive medium (loam soil) in a nonequilibrium situation, is different from volatilization from an inert surface or from the chemical's own surface. Therefore, the environmental volatilization index assigned to pesticides studied in this manner may or may not parallel a chemical's vapor pressure. By this method, captan rated a volatilization index of 2, indicating an estimated median vapor loss from treated areas of 1.8 lb/acre/year. This index number indicates that the propensity for volatilization of captan from treated fields is in the intermediate range, compared to many other pesticides.

Leaching index numbers for pesticides indicate the approximate distance that the chemical would move through the standardized loam soil profile under an annual rainfall of 59 in. Under these conditions, captan rated a leaching index number of 1, indicating movement of less than 4 in.

This data, as well as the model ecosystem studies by the Illinois Natural History Survey (1973) reviewed in the preceding subsection, indicates that under field conditions, residues of intact captan are unlikely to migrate away from target areas to a significant extent. Captan is degraded rapidly in soil and in water under environmental conditions. Its residual effectiveness on treated plants lasts for about 3 to 7 days. Little information is available on the nature, toxicity, persistency, and environmental fate and effects of the degradation products of captan.

Captan has been in large-scale commercial use in the United States and in many other countries for about 20 years. No environmental problems have been attributed to its use as a fungicide to this date.

[1/] von Rumker, R., and F. Horay, Pesticide Manual, Vol. I, Department of State, Agency for International Development (1972).

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART D. PRODUCTION AND USE

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Registered Uses

Federally Registered Uses - Captan is a contact fungicide that is effective against a fairly broad spectrum of plant-pathogenic fungi. It is registered and reocmmended in the United States for use on more than 80 different crops. Tolerances for captan residues have been established on 67 raw agricultural commodities, ranging from 2 to 100 ppm. Ten of these tolerances are currently designated as "interim tolerances." It is also registered for use on surfaces and as a preservative for textiles, plastics, cosmetics, etc.

The registered uses of captan by crops, established tolerances, dosage rates, and use limitations are summarized in the "EPA Compendium of Registered Pesticides."1/

The registered uses of captan are detailed in this section in a set of two tables as follows:

Table 19: Summary of Registered Use of Captan, a listing of crops, common and scientific names of the fungal organisms affecting each crop, rates of application, and limitations.

Table 20: Registered uses of captan 50% wettable powder (one of the most commonly used formulations of captan) by crops, diseases controlled on each crop, recommended dosage rates, and general and specific directions for, and limitations of use.

1/ U.S. Environmental Protection Agency, EPA Compendium of Registered Pesticides, Vol. II: Fungicides and Nematicides, pp. II-C-2.1-2.11 (1973).

Table 19. SUMMARY OF REGISTERED USES OF CAPTAN*

Crop or Site of Application	Disease or Organism Controlled	Rates[a/] AI[b/] Lb/100 Gal or Lb/Acre	Limitations
I. Foliage and Fruit Applications			
A. Agricultural Crops - Fruit and Nut Crops			
Almonds	Blossom Blight (Monilinia)	1.0	Do not apply within 12 days of harvest Do not feed hulls to dairy animals or cattle 2.0 ppm on almonds 100.0 ppm on almond hulls.
	Brown Rot, Twig Blight (Monilinia)	1.0	do[c/]
	Scab (Cladosporium)	1.0	do
	Shothole (Coryneum)	1.0	do
Apples	Bitter Rot (Glomeralla)	1.0	No time limitation. 25.0 ppm
	Black Pox (Helminthosporium)	1.0	do
	Black Rot (Physalospora)	1.0	do
	Botryosphaeria (White Rot)	1.0	do
	Botrytis Rot	1.0	do

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*Tabulation prepared by Eugene M. Wilson and E. N. Pelletier, Criteria and Evaluation Division, Office of Pesticides Programs, from EPA Compendium of Registered Pesticides, Vol. II, *op. cit.* (1973).

a/ Rates are expressed as follows: 1) AI Lb/100 Gal or Lb/Acre for Foliage and Fruit Applications and Soil Applications; 2) AI 100 Lb Seed for Seed Applications; 3) Lb or % for Miscellaneous Agricultural Uses.

b/ AI = Active Ingredient.

c/ do = ditto as above

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
Apples (Cont'd.)	Brooks Spot (Mycosphaerella)	0.25-1.0	do
	Bullseye Rot (Neofabraea)	1.0	do
	Cedar-Apple Rust (Gynosporangium)	1.0	do
	Flyspeck (Microthyriella)	0.25-1.0	do
	Frogeye Leaf Spot (Physalospora)	1.0	do
	Quince Rust (Gymnosporangium)	1.0	
	Scab (Venturia)	0.75-1.0	do
	Sooty Blotch (Gloeodes)		do
	Storage Rots	1.0-1.2	Apply as a post-harvest dip or spray. Limits: 0.12% solution. 25.0 ppm
Apricots	Brown Rot, twig blight (Monilinia)	1.0	No time limit. 50.0 ppm.
	Green Rot, Jacket rot	1.0	do
	Molds	1.0-1.2	Post-harvest spray or dip. 50 ppm
	Storage Rots	do	do

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
Avocados	Blotch, Cercospora Spot	1.0	25.0 ppm. No time limits.
Blackberry	Anthracnose (Elsinae)	1.0	No time limitation. 25.0 ppm
	Fruit Rot	1.0	do
Blueberries	Botrytis Blight, (Graymold)	1.0	No time Limitation. 25.0 ppm
	Mummy Berry (Monilinia)	1.0	do
Cherries	Brown Rot (Monilinia)	1.0	No time Limitation. 100.0 ppm.
	Leaf Spot (Coccomyces)	1.0-2.0	do
	Postharvest Decay	1.0-1.2	100.0 ppm
Citrus (All)	Brown Rot (Phytophythora)	1.0-2.0	No time limitation. Do not feed byproducts to diary animals or animals used for meat. 25.0 ppm.
	Post-harvest Decay	1.0 2.0	Dip or Spray 25.0 ppm
Cranberries	Blotch rot (Acanthorhyncus)	1.0	do
	Guigardia blight	1.0	do
	Storage rots	1.0	do

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
	Twig Blight (Lophodermium)	1.0	No time limitation. 25.0 ppm
Dewberry	Anthracnose (Elsinoe)	1.0	No time limitation. 25.0 ppm
	Fruit Rot	1.0	do
Grapes	Black Rot (Guigardia)	1.0	No time limitation. 50.0 ppm
	Botrytis Bunchrot	1.0	
	Dead Arm (Cryptosporella)	1.0	do
	Storage Rots	1.0	do
Grapes (Raisins)	Mold, While Drying	1.0-1.5	Do not apply within 5 days of a pre-harvest application of captan, 100.0 ppm.
Mango	Cercospora Leaf Spot	1.0	50.0 ppm
	Molds and Storage Rots	1.0-1.2	Dip or spray. 50.0 ppm
Nectarines	Brown Rot (Monilinia)	1.0	No time limitations. 50.0 ppm
	Coryneum Blight (shothole)	1.0	do
	Post-harvest Diseases	1.0-1.2	Dip or spray 50.0 ppm
	Scab (Cladosporium)	1.0	No time limitation 50.0 ppm

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
Oranges and Tangelos	Brown Rot (Phythophthora)	1.0	Do not apply after fruit size exceeds 0.5 inches in diameter. 50.0 ppm
	Melanose (Diaporthe)	do	do
	Scab (Elsinoe)	do	do
Peaches	Brown Rot Blossom Blight (Monilinia)	1.0	No time limitation or 6.0 lbs/A and do not apply within 1 day of harvest. 50.0 ppm
	Post-harvest Decay	1.0-1.2	Dip or spray 50.0 ppm
	Rhizopus Rot	1.0	No time limitation or 6.0 lbs/A. Do not apply within 1 day of harvest 50.0 ppm.
	Scab (Cladosporium)	1.0	do
	Shothole Blight (Coryneum)	1.0	do
	Crown Gall	2.0	None (non-food use) Use in Mixture with Sodium hypochlorite 200 ppm Chloride.
Pears	Fruit Spot (Leptothyrium)	1.0	No time limitation. 25.0 ppm
	Post-harvest Diseases	1.0-1.2	Dip or spray 25.0 ppm.

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
	Scab (Venturia)	1.0	No time limitation. 25.0 ppm
Pineapples	Heart Rot(Phytophthora)	5.0	No time limitation. 25.0 ppm
	Root Rot(Phytophthora)	2.0	do
	Storage and Transit Rot	5.0	Dip or spray 25.0 ppm
Plums and Prunes	Brown Rot (Monilinia)	1.0	No time limitation. 50.0 ppm
	Russet or lacy scab (Cladosporium)	1.0	do
Quince	Brown Rot (Monilinia)	5.0	Do not apply within 7 days of harvest 25.0 ppm
	Scab (Venturia)	5.0	do
Raspberry	Anthracnose (Elsinoe)	1.0	No time limitation. 25.0 ppm
	Botrytis Blight	1.0	do
	Fruit Rot	1.0	do
	Spur Blight (Didymella)	1.0	do
Strawberry	Botrytis Rot	1.5	No time limitation. 25.0 ppm
	Leaf Spots	1.5	do

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
I.B. Agricultural Crops - Vegetable Crops			
Asparagus	Botrytis Blight, Phoma Rot, Penicillium Rot, Fusarium Rot	1.5	Preplanting dip. Non-food use
Beans (Field and Snap)	Anthracnose (Collectotrichum)	0.5	No time limitation. 25.0 ppm
	Downy Mildew(Phytophthora)	0.5	do
	Rust (Uromyces)	0.5	do
Beets	Alternaria Leaf Spot	1.0	No time limitation. 2.0 ppm on roots, 100.0 ppm on greens.
	Cercospora Leaf Spot	1.0	do
	Leaf Spots (septoria)	1.0	do
Cantaloupe, Cucumbers, Honeydew Melon, Pumpkins, Squash, (Summer and Winter) and Watermelon	Angular Leaf Spot (Psedomonas)	1.5	No time limitation. 25.0 ppm
	Anthracnose (Marssonina)	1.5	No time limitation. 25.0 ppm
	Downy Mildew (Pseudoperonospora)	1.5	do
	Post-harvest Decay	1.25	As dip or spray 25.0 ppm

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
Carrots	Alternaria Blight (Late Blight)	1.0	No time limitation. 2.0 ppm
	Cercospora Blight (Early Blight)	1.0	do
	Septoria Leaf Spot	1.0	do
Celery	Late Blight (Septoria)	1.0	No time limitation. 50.0 ppm
	Pink Rot (Sclerotinia)	1.0	do
Corn (Sweet)	Helminthosporium (Leaf Blight)	0.75	2.0 ppm
Cucumbers (see Cantaloupes)			
Eggplant	Anthracnose (Colletotrichum)	1.0	No time limitation. 25.0 ppm
	Fruit Rot	1.0	do
	Early Blight (Alternaria)	1.0	do
	Phomopsis Blight	1.0	do
Lettuce	Downy Mildew (Bremia)	1.0	No time limitation. 100.0 ppm
Onions (Green and Bulb-pre-harvest)	Downy Mildew (Peronospora)	1.0	No time limitation. 50.0 ppm on green onions, 25.0 ppm on dry

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
	Purple Blotch (Alternaria)	1.0	do No time limitation.
	Molds, Storage Rots	1.25	do
Peppers, Pimentos	Anthracnose (Colletotrichum)	1.5	No time limitation. 25.0 ppm
	Cercospora Leaf Spot and Stem-End Rot	1.5	do
Potatoes	Early Blight (Alternaria)	2.0-4.0	No time limitation. 25.0 ppm
	Late Blight (Phytophthora)	2.0-4.0	do
	Storage rots	1.25	25.0 ppm
	Seed-piece Treatment (Browneye, Damping-off and Verticillium)	0.5-1.5	25.0 ppm
Rhubard (Greenhouse)	Botrytis(Leaf rot)	1.0	No time limitation. 25.0 ppm
Spinach	Downy Mildew (Peronospora)	1.0	100.0 ppm
Tomatoes	Anthracnose (Collettotrichum)	2.0	No time limitation. 25.0 ppm
	Early Blight (Alternaria)	2.0	do
	Grey Leaf Spot (Stemphylium)	2.0	do

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
	Late Blight (Phytophthora)	2.0	do
	Septoria Leaf Spot	2.0	do
I.C. Agricultural Crops Ornamental Crops			
Azaleas	Petal Blight (Ovulinia)	2.0	None
	Damping-off	2.0	None
Begonias	Damping-off	2.0	None
	Powdery mildew (Erysiphe)	0.11-0.22	
Camellias	Petal Blight (Sclerotinia)	0.5	None
Carnations	Alternaria Leaf Spot	1.0	None
	Damping-off	2.0	None
	Rust(Uromyces)	1.0	None
Chrysanthemum	Botrytis Flower Blight	1.0	None
	Damping-off	2.0	None
	Septoria Leaf Spot	1.0	None
Dichondra	White mold(Sclerotium)	1.0	None
Gladiolus	Corm rot	2.0-7.5	None
Roses	Black Spot(Diplocarpon)	1.0	None
	Botrytis Blight	1.0	None

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
Grasses	Brown Patch(Rhizoctonia)	1.0-2.0	Non-pastured areas only
	Copper Spot(Gloeocercospora)	do	do
	Damping-off	do	do
	Leaf spots	do	do
	Melting-out (Helminthosporium)	do	do
	Seedling Blight	do	do
Hollyhock	Anthracnose (Colletotrichum)	2.1/A	None
Lilacs	Anthracnose	2.1/A	None
Snapdragon	Anthracnose	2.1/A	None
Spirea	Anthracnose	2.1/A	None
Stock	Botrytis Blight	4.0-5.0/A	None
II Soil Application			
A. Agricultural Crops-Vegetable Crops			
Beets	Root Rots	3.3/A	preplanting 2.0 ppm on roots
Cantaloupe, Cucumber, Honeydew Melon Pumpkin, Squash and Watermelon	Damping-off Root rots	1.0	preplanting 25.0 ppm

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
Celery	Damping-off	1.0	preplanting 50.0 ppm
Collards	Damping-off	7.5/A	preplanting 2.0 ppm
Corn (sweet)	Damping-off	6.0/A	preplanting 2.0 ppm
	Root rot	6.0/A	do
Cucumbers	Damping-off	1.0	do
	Root-Rot	1.0	do
Eggplant	Damping-off	5.0-6.0	do
Kale, Collards Mustard, Rutabagas, Turnips	Damping-off	7.5/A	preplanting 2.0 ppm on greens 2.0 ppm on roots
Peppers	Damping-off	1.0	preplanting 25.0 ppm
Spinach	Damping-off	2.0-6.0/A	preplanting 100.0 ppm
Tomatoes	Damping-off Root Rot	5.0-7.5/A	preplanting
II. B. Agricultural Crops-Field Crops			
Cotton	Damping-off	4.0-6.0/A	planting 2.0 ppm
Soybeans	Damping-off	2.0-6.0/A	do
II. C. Agricultural Crops-Ornamental Crops			
Azaleas	Petal Blight (Ovulinia)	2.0	none
Flowers	Seed & Root Rot	1.0	None

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI Lb/100 Gal or Lb/Acre	Limitations
Trees	Damping-off	1.0	None
Grasses	Damping-off	1.0	None
III. **Seed Applications**			
		AI 100 Lb Seed	
Alfalfa	Damping-off	0.4-6.0	Do not use treated seed for food, feed or oil purposes non-food use.
Barley	Seedling Diseases	0.6-2.0	do
Beans	Seedling Diseases	0.2-3.0	do
Beets(Sugar)	Seedling Diseases	0.6-9.6	do
Bluegrass	Seedling Diseases	2.2-6.0	do
Broccoli	Seedling Diseases	0.4-2.25	do
Brussels Sprouts	Seedling Diseases	0.4-2.25	do
Cabbage	Seedling Diseases	0.4-2.25	do
Cantaloupe	Seedling Diseases	0.8-2.25	do
Cauliflower	Seedling Diseases	0.4-2.25	do
Clover	Seedling Diseases	2.2-6.0	do
Collards	Seedling Diseases	0.4-1.8	do
Corn(Field)	Seedling Diseases	0.5-1.8	do
Corn(Sweet)	Seedling Diseases	0.8-3.75	do

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI 100 Lb Seed	Limitations
Cotton	Seedling Diseases	0.75-4.0	do
Cowpeas	Seedling Diseases	0.8-2.25	do
Crucifers	Seedling Diseases	0.4-1.8	do
Cucumbers	Seedling Diseases	0.7-2.2	do
Flax	Seedling Diseases	1.0-2.2	do
Grasses	Seedling Diseases	2.2-9.0	do
Kale	Seedling Diseases	0.4	do
Lespedeza	Seedling Diseases	2.2-6.0	do
Milo	Seedling Diseases	0.8-3.0	do
Muskmelon	Seedling Diseases	0.5-1.5	do
Mustard	Seedling Diseases	0.3-2.2	do
Oats	Seedling Diseases	0.6-5.63	do
Onions	Seedling Diseases	0.75-16.0	do

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates AI 100 Lb Seed	Limitations
Peanuts	Seedling Diseases	0.4-6.0	do
Pumpkins	Seedling Diseases	0.5-1.54	do
Peas	Seedling Diseases	0.8-3.0	do
Peppers	Seedling Diseases	0.8-2.25	do
Rice	Seedling Diseases	0.9-3.75	do
Rye	Seedling Diseases	0.6-3.2	do
Safflower	Seedling Diseases	0.3-1.9	do
Sesame	Seedling Diseases	0.75-1.6	do
Sorghum	Seedling Diseases	0.5-2.4	do
Soybeans	Seedling Diseases	0.7-3.0	do
Spinach	Seedling Diseases	1.8-4.5	do
Squash	Seedling Diseases	0.5-1.54	do
Swiss Chard	Seedling Diseases	3.4-9.0	do

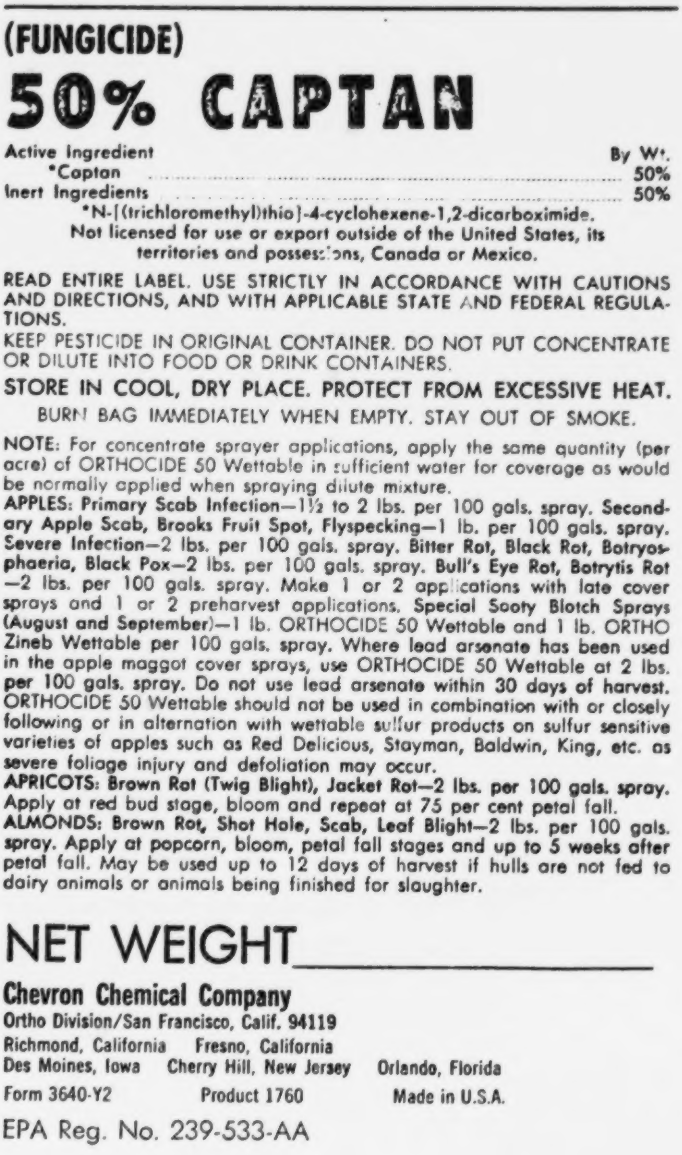
Table 19. (Continued)

Crop of Site of Application	Disease or Organism Controlled	Rates AI 100 Lb Seed	Limitations
Tomato	Seedling Diseases	0.8	do
Trefoil	Seedling Diseases	2.2-6.0	do
Turnips	Seedling Diseases	0.4-1.5	do
Watermelons	Seedling Diseases	0.5-1.54	do
Wheat	Seedling Diseases	0.4-3.0	do
IV. Miscellaneous Agricultural Uses		Lb or %	
Packing Boxes	Storage Rots	1.0/100 gallons	None
Soil and Greenhouse Bench Preplanting Treatment	Damping-off Root Rots	5.0-6.0 lbs/A	None
House Plants	non-specified	Variable	None
Home Gardens	do	do	As with specific agricultural uses

Table 19. (Continued)

Crop or Site of Application	Disease or Organism Controlled	Rates Lb or %	Limitations
IV. Home Environment - Inside and Outside			
Paints	Mildew	1.0 oz/gal	Control on painted surfaces
Surfaces	Fungi	0.31% by weight	None
V. Industrial Uses			
Cosmetics and Pharmaceuticals	Fungi	0.1-0.5% by weight	None
Lacquers, Paints (oil based)	Fungi	0.52-2.1% by weight	None
Paper	Mold & Mildew	0.15-0.90% by weight	None
Paste (Wallpaper Flower)	Mold & Mildew	0.225% by weight	None
Plasticizers (Fungicidal Plastics)	Fungi	0.225% by weight	None
Polyethylene	Mold & Mildew	0.44-1.74% by weight	None
Rubber Stabilizer	Mold & Mildew	0.44-1.75% by weight	None
Textiles	Molds & Mildew	0.90-1.7% by weight	None
Vinyl	Mildew	0.44-0.90% by weight	None

Table 20. REGISTERED USES OF CAPTAN 50% WETTABLE POWDER-- CROPS AND OTHER USES, DISEASES CONTROLLED DOSAGE RATES, AND USE LIMITATIONS



(FUNGICIDE)

50% CAPTAN

Active Ingredient	**By Wt.**
***Captan**	**50%**
Inert Ingredients	**50%**

***N-[(trichloromethyl)thio]-4-cyclohexene-1,2-dicarboximide.**
Not licensed for use or export outside of the United States, its territories and possessions, Canada or Mexico.

READ ENTIRE LABEL. USE STRICTLY IN ACCORDANCE WITH CAUTIONS AND DIRECTIONS, AND WITH APPLICABLE STATE AND FEDERAL REGULATIONS.

KEEP PESTICIDE IN ORIGINAL CONTAINER. DO NOT PUT CONCENTRATE OR DILUTE INTO FOOD OR DRINK CONTAINERS.

STORE IN COOL, DRY PLACE. PROTECT FROM EXCESSIVE HEAT.

BURN BAG IMMEDIATELY WHEN EMPTY. STAY OUT OF SMOKE.

NOTE: For concentrate sprayer applications, apply the same quantity (per acre) of ORTHOCIDE 50 Wettable in sufficient water for coverage as would be normally applied when spraying dilute mixture.

APPLES: Primary Scab Infection—1½ to 2 lbs. per 100 gals. spray. **Secondary Apple Scab, Brooks Fruit Spot, Flyspecking**—1 lb. per 100 gals. spray. **Severe Infection**—2 lbs. per 100 gals. spray. **Bitter Rot, Black Rot, Botryosphaeria, Black Pox**—2 lbs. per 100 gals. spray. **Bull's Eye Rot, Botrytis Rot**—2 lbs. per 100 gals. spray. Make 1 or 2 applications with late cover sprays and 1 or 2 preharvest applications. **Special Sooty Blotch Sprays (August and September)**—1 lb. ORTHOCIDE 50 Wettable and 1 lb. ORTHO Zineb Wettable per 100 gals. spray. **Where lead arsenate has been used in the apple maggot cover sprays, use ORTHOCIDE 50 Wettable at 2 lbs. per 100 gals. spray. Do not use lead arsenate within 30 days of harvest.** ORTHOCIDE 50 Wettable **should not be used in combination with or closely following or in alternation with wettable sulfur products on sulfur sensitive varieties of apples such as Red Delicious, Stayman, Baldwin, King, etc. as severe foliage injury and defoliation may occur.**

APRICOTS: Brown Rot (Twig Blight), Jacket Rot—2 lbs. per 100 gals. spray. Apply at red bud stage, bloom and repeat at 75 per cent petal fall.

ALMONDS: Brown Rot, Shot Hole, Scab, Leaf Blight—2 lbs. per 100 gals. spray. Apply at popcorn, bloom, petal fall stages and up to 5 weeks after petal fall. May be used up to 12 days of harvest if hulls are not fed to dairy animals or animals being finished for slaughter.

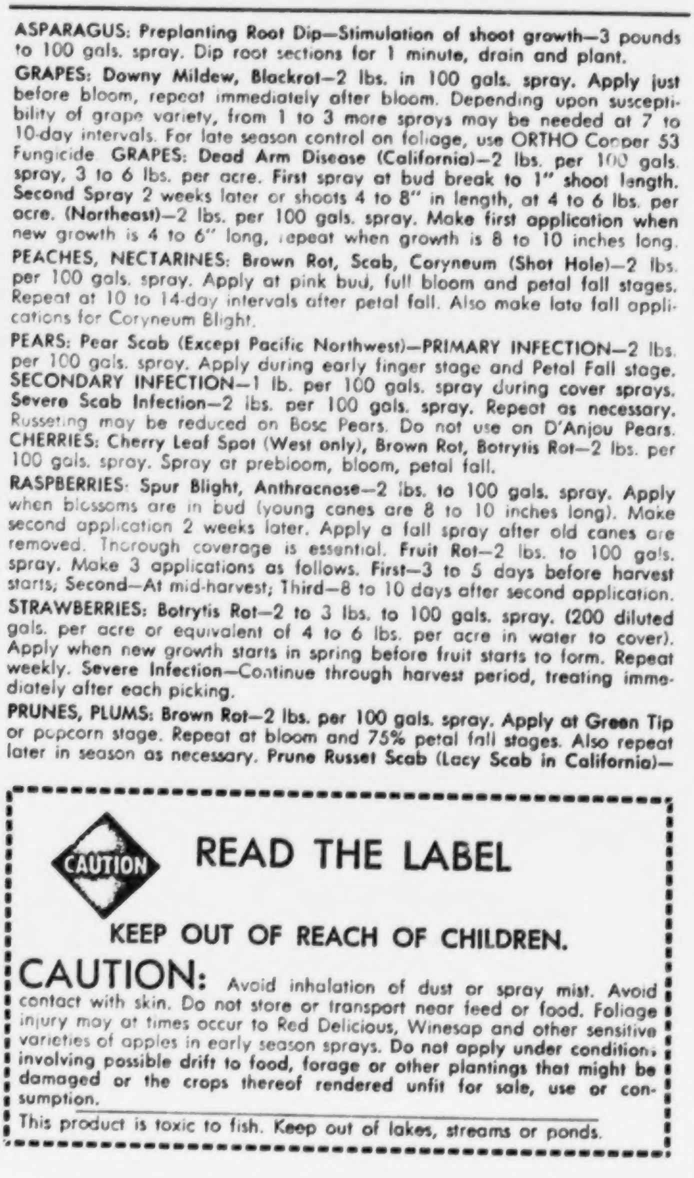
NET WEIGHT________________

Chevron Chemical Company
Ortho Division/San Francisco, Calif. 94119
Richmond, California Fresno, California
Des Moines, Iowa Cherry Hill, New Jersey Orlando, Florida
Form 3640-Y2 Product 1760 Made in U.S.A.

EPA Reg. No. 239-533-AA

Source: Chevron Chemical Company, San Francisco, Calif.

Table 20. (Continued)



ASPARAGUS: Preplanting Root Dip—Stimulation of shoot growth—3 pounds to 100 gals. spray. Dip root sections for 1 minute, drain and plant.

GRAPES: Downy Mildew, Blackrot—2 lbs. in 100 gals. spray. Apply just before bloom, repeat immediately after bloom. Depending upon susceptibility of grape variety, from 1 to 3 more sprays may be needed at 7 to 10-day intervals. For late season control on foliage, use ORTHO Copper 53 Fungicide. **GRAPES: Dead Arm Disease (California)**—2 lbs. per 100 gals. spray, 3 to 6 lbs. per acre. **First spray at bud break to 1" shoot length. Second Spray** 2 weeks later or shoots 4 to 8" in length, at 4 to 6 lbs. per acre. **(Northeast)**—2 lbs. per 100 gals. spray. **Make first application when** new growth is 4 to 6" long, repeat when growth is 8 to 10 inches long.

PEACHES, NECTARINES: Brown Rot, Scab, Coryneum (Shot Hole)—2 lbs. per 100 gals. spray. Apply at pink bud, full bloom and petal fall stages. Repeat at 10 to 14-day intervals after petal fall. Also make late fall applications for Coryneum Blight.

PEARS: Pear Scab (Except Pacific Northwest)—PRIMARY INFECTION—2 lbs. per 100 gals. spray. Apply during early finger stage and Petal Fall stage. **SECONDARY INFECTION**—1 lb. per 100 gals. spray during cover sprays. **Severe Scab Infection**—2 lbs. per 100 gals. spray. Repeat as necessary. Russeting may be reduced on Bosc Pears. Do not use on D'Anjou Pears. **CHERRIES: Cherry Leaf Spot (West only), Brown Rot, Botrytis Rot**—2 lbs. per 100 gals. spray. Spray at prebloom, bloom, petal fall.

RASPBERRIES: Spur Blight, Anthracnose—2 lbs. to 100 gals. spray. Apply when blossoms are in bud (young canes are 8 to 10 inches long). Make second application 2 weeks later. Apply a fall spray after old canes are removed. Thorough coverage is essential. **Fruit Rot**—2 lbs. to 100 gals. spray. Make 3 applications as follows. **First**—3 to 5 days before harvest starts; **Second**—At mid-harvest; **Third**—8 to 10 days after second application.

STRAWBERRIES: Botrytis Rot—2 to 3 lbs. to 100 gals. spray. (200 diluted gals. per acre or equivalent of 4 to 6 lbs. per acre in water to cover). Apply when new growth starts in spring before fruit starts to form. Repeat weekly. **Severe Infection**—Continue through harvest period, treating immediately after each picking.

PRUNES, PLUMS: Brown Rot—2 lbs. per 100 gals. spray. **Apply at Green Tip** or popcorn stage. Repeat at bloom and 75% petal fall stages. Also repeat later in season as necessary. **Prune Russet Scab (Lacy Scab in California)**—

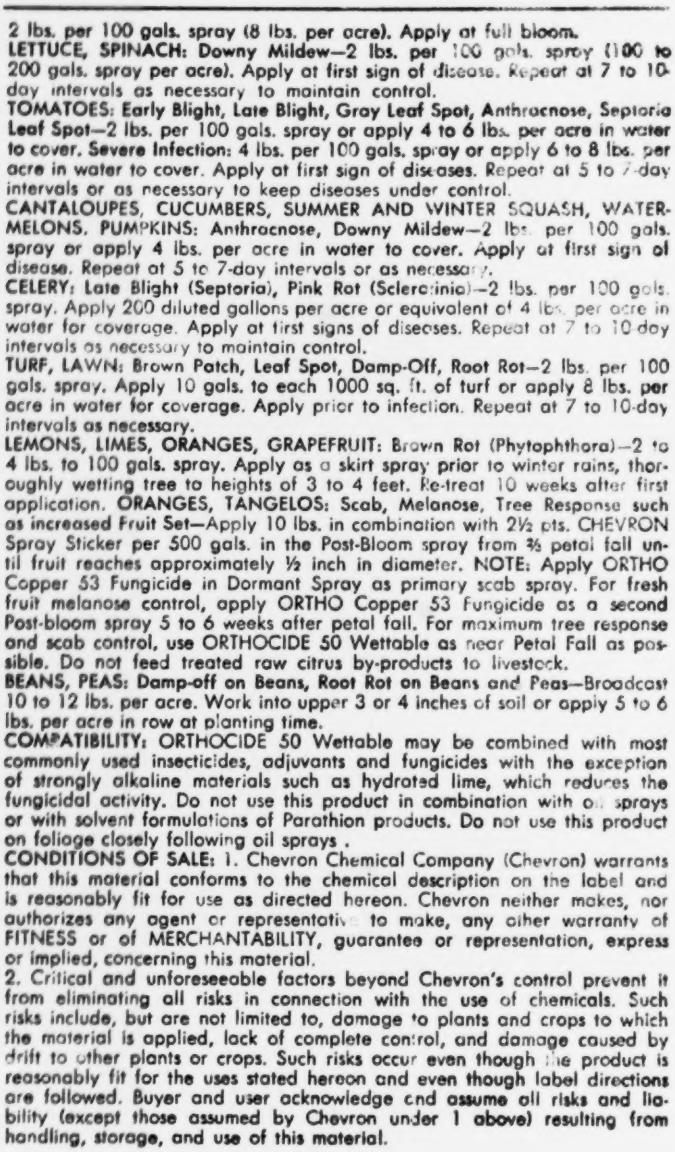
READ THE LABEL

KEEP OUT OF REACH OF CHILDREN.

CAUTION: Avoid inhalation of dust or spray mist. Avoid contact with skin. Do not store or transport near feed or food. Foliage injury may at times occur to Red Delicious, Winesap and other sensitive varieties of apples in early season sprays. **Do not apply under conditions involving possible drift to food, forage or other plantings that might be damaged or the crops thereof rendered unfit for sale, use or consumption.**

This product is toxic to fish. Keep out of lakes, streams or ponds.

Table 20. (Continued)



2 lbs. per 100 gals. spray (8 lbs. per acre). Apply at full bloom.

LETTUCE, SPINACH: Downy Mildew—2 lbs. per 100 gals. spray (100 to 200 gals. spray per acre). Apply at first sign of disease. Repeat at 7 to 10-day intervals as necessary to maintain control.

TOMATOES: Early Blight, Late Blight, Gray Leaf Spot, Anthracnose, Septoria Leaf Spot—2 lbs. per 100 gals. spray or apply 4 to 6 lbs. per acre in water to cover. **Severe Infection:** 4 lbs. per 100 gals. spray or apply 6 to 8 lbs. per acre in water to cover. Apply at first sign of diseases. Repeat at 5 to 7-day intervals or as necessary to keep diseases under control.

CANTALOUPES, CUCUMBERS, SUMMER AND WINTER SQUASH, WATERMELONS, PUMPKINS: Anthracnose, Downy Mildew—2 lbs. per 100 gals. spray or apply 4 lbs. per acre in water to cover. Apply at first sign of disease. Repeat at 5 to 7-day intervals or as necessary.

CELERY: Late Blight (Septoria), Pink Rot (Sclerotinia)—2 lbs. per 100 gals. spray. Apply 200 diluted gallons per acre or equivalent of 4 lbs. per acre in water for coverage. Apply at first signs of diseases. Repeat at 7 to 10-day intervals as necessary to maintain control.

TURF, LAWN: Brown Patch, Leaf Spot, Damp-Off, Root Rot—2 lbs. per 100 gals. spray. Apply 10 gals. to each 1000 sq. ft. of turf or apply 8 lbs. per acre in water for coverage. Apply prior to infection. Repeat at 7 to 10-day intervals as necessary.

LEMONS, LIMES, ORANGES, GRAPEFRUIT: Brown Rot (Phytophthora)—2 to 4 lbs. to 100 gals. spray. Apply as a skirt spray prior to winter rains, thoroughly wetting tree to heights of 3 to 4 feet. Re-treat 10 weeks after first application. **ORANGES, TANGELOS:** Scab, Melanose, Tree Response such as increased Fruit Set—Apply 10 lbs. in combination with 2½ pts. CHEVRON Spray Sticker per 500 gals. in the Post-Bloom spray from ⅔ petal fall until fruit reaches approximately ½ inch in diameter. NOTE: Apply ORTHO Copper 53 Fungicide in Dormant Spray as primary scab spray. For fresh fruit melanose control, apply ORTHO Copper 53 Fungicide as a second Post-bloom spray 5 to 6 weeks after petal fall. For maximum tree response and scab control, use ORTHOCIDE 50 Wettable as near Petal Fall as possible. Do not feed treated raw citrus by-products to livestock.

BEANS, PEAS: Damp-off on Beans, Root Rot on Beans and Peas—Broadcast 10 to 12 lbs. per acre. Work into upper 3 or 4 inches of soil or apply 5 to 6 lbs. per acre in row at planting time.

COMPATIBILITY: ORTHOCIDE 50 Wettable may be combined with most commonly used insecticides, adjuvants and fungicides with the exception of strongly alkaline materials such as hydrated lime, which reduces the fungicidal activity. Do not use this product in combination with oil sprays or with solvent formulations of Parathion products. Do not use this product on foliage closely following oil sprays .

CONDITIONS OF SALE: 1. Chevron Chemical Company (Chevron) warrants that this material conforms to the chemical description on the label and is reasonably fit for use as directed hereon. Chevron neither makes, nor authorizes any agent or representative to make, any other warranty of FITNESS or of MERCHANTABILITY, guarantee or representation, express or implied, concerning this material.

2. Critical and unforeseeable factors beyond Chevron's control prevent it from eliminating all risks in connection with the use of chemicals. Such risks include, but are not limited to, damage to plants and crops to which the material is applied, lack of complete control, and damage caused by drift to other plants or crops. Such risks occur even though the product is reasonably fit for the uses stated hereon and even though label directions are followed. Buyer and user acknowledge and assume all risks and liability (except those assumed by Chevron under 1 above) resulting from handling, storage, and use of this material.

Table 20 is a copy of the label of a widely used captan formulation, registered by the Ortho Division of Chevron Chemical Company, the largest formulator and marketer of captan (EPA Registration Number 239-533-AA). As this label indicates, the directions for use of captan are quite complex and differ considerably from crop to crop.

The registration data on captan presented in Tables 19 and 20 indicate that this product is a broad spectrum fungicide useful in the control of foliage diseases of many fruit, vegetable and ornamental cuttings and bulbs; for the control of some diseases on turf and lawns; as a seed protectant; and as a potato seed piece treatment for control of rots.

State Regulations - Captan is one of the less toxic synthetic pesticides, rated "slightly toxic" for labeling purposes. Captan is not currently subject to specific use restrictions under state pesticide laws or regulations. Seed treatment uses of captan may be subject to state laws covering this area, including such matters as coloring and labeling of treated seeds, etc.

Production and Domestic Supply

Volume of Production - According to the United States Tariff Commission's synthetic organic reports, there has been only one basic source of production of captan in the United States in recent years, up to and including 1972, i.e., Stauffer Chemical Company's Calhio Chemicals Division plant located in Perry, Ohio (a unit operated jointly by Stauffer and the Ortho Division of Chevron Chemical Company).

In the Tariff Commission's reports, the production and sales volumes of captan are not reported individually. In the most recent report, covering calendar year 1972[1/], captan is included in a category identified as "all other cyclic fungicides." In addition to captan, this group includes six other specific cyclic fungicides; tri- and tetra-chlorophenols; and additional, unspecific cyclic fungicides. The production volume for this composite group in 1972 was reported at 45,360,000 lb of active ingredients.

Through a process of careful analysis of the production and use patterns of all organic fungicides in this group, supported by information from trade sources, Midwest Research Institute developed estimates on the volume of production of all major products in the group. The estimated volume of production of captan in 1972 is 17 million pounds of active ingredient (AI).

[1/] U.S. Tariff Commission, Synthetic Organic Chemicals, U.S. Production and Sales, 1972, TC Publication 681 (1973).

Imports - Imports of pesticides that are classified as "benzenoid chemicals" (this group would include captan) are reported in a 1973 U.S. Tariff Commission annual report.[1] According to the report, there were no imports of captan into the United States in 1972.

Exports - Pesticide exports are reported by the Bureau of the Census annually. Technical (unformulated) captan is included in this report in Schedule B, Section 512.0610, a category including all technical synthetic organic fungicides. Formulations of captan are included in Schedule B, Section 599.2055, entitled "Captan and Mercury Fungicidal Preparations, Except Household and Industrial."[2]

Total exports of organic fungicides in these two categories for 1972 were as follows:

Section 512.0610 (Technical Synthetic Organic Fungicides)
8,111,219 lb.

Section 599.2055 (Captan and Mercury Fungicide Formulations)
761,875 lb.

To derive the 1972 export volume of captan from these composite totals, we made a thorough analysis of these two pesticide export categories by unit dollar values and by countries of destination. In the next step this information was matched against our knowledge of the crop protection problems and the pesticide trading patterns of the countries of destination. Additional information was obtained from trade contacts, from the U.S. Agency for International Development (AID), and from other sources. Based on all data and information obtained in this manner, Midwest Research Institute estimates the 1972 export volume of captan at 1.0 million pounds AI.

Domestic Supply - The estimated domestic supply of captan in the United States in 1972 was as follows, based on the data presented in the preceding three sections:

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[1] U.S. Tariff Commission, Imports of Benzenoid Chemicals and Products, TC Publication 601 (1973).

[2] U.S. Bureau of the Census, U.S. Exports, Schedule B, Commodity by Country, Report FT 410.

U.S. Production	17.0 Million lb AI
Imports	None or negligible
Exports	1.0 Million lb AI
Domestic Supply	16.0 Million lb AI

Comparable estimates for 1973 cannot be made at this time because the U.S. Tariff Commission report on the production and sales of pesticides in 1973 will not be published until the fall of 1974.

Formulations - Captan is available to users in the United States in a great variety of dry formulations, i.e., wettable powders and dusts of various concentrations. An aqueous suspension captan formulation is available on the market at the present time.

The basic producer of captan, Stauffer Chemical Company, sells a substantial share of its production to formulator-customers in the form of technical or manufacturing concentrates. The largest formulator by far is the Ortho Division of Chevron Chemical Company. Ortho and some other formulators then prepare and sell formulations containing captan under their own labels and brand names to end users, either directly, or through wholesalers and/or retailers. Stauffer Chemical Company also prepares and markets formulated captan products.

Frear (1972)[1] lists the following pesticide products containing captan as the only active ingredient:

13 Dust formulations (ranging in concentration from 5.0-25.0%; 7.5% apparently the most popular strength)
1 Dust base concentrate (90.0%)
6 Wettable powders (five of these 50% AI; one 80%)
2 75% Seed treatment formulations (for slurry treaters)
2 Manufacturing concentrates for industrial and pharmaceutical purposes.

In addition to these products containing captan as the only active ingredient, a number of combination formulations, primarily dusts, are listed in which captan is combined with other fungicides and/or insecticides, for foliar application, seed treatment, and related uses.

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[1] Frear, D. E. H., Pesticide Handbook-Entoma, 24th ed., College Science Publishers, State College, Pa. (1972).

Since the 1972 edition of the *Pesticide Handbook* was put together, a number of additional captan formulations have become available, especially seed treatment products. For instance, as of the spring of 1974, the Ortho Division of Chevron Chemical Company carried the following captan products in its line:

Sprayable formulations for foliar applications:

Captan 50% wettable powder
Captan 80% wettable powder
Captan 40% - zineb 30% wettable powder
Captan 15% - malathion 7.5% - methoxychlor 15% wettable powder

Dust formulations for foliar applications:

Fungicides only:

Captan dusts containing 5, 7.5, 10, and 15% of AI
Captan-sulfur combination dusts in seven different ratios i.e., 5-50; 7.5-25; 10-10; 10-25; 10-50; 15-25; and 15-40
Captan 10% - Botran 5% - sulfur 40% dust

Fungicide - insecticide combinations:

Captan 5% - naled 6% dust
Captan 10% - naled 4% dust
Captan 5% - endosulfan 2% dust
Captan 5% - Omite 3% dust
Captan 5% - naled 3% - carbaryl 7.5% - sulfur 25% dust
Captan 5% - methoxychlor - 5% - rotenone 0.75% - other cube resins 0.75% dust

Seed protectant and soil treatment formulations:

Fungicide(s) only, seed treatment:

Captan 5%, 10% and 15% dusts for potato seed piece treatment
Captan 25% dusts for soybean and peanut seed protection
Captan 65% seed protectant dust (peas)
Captan 75% seed protectant dust (many crops)
Captan 75% seed protectant for slurry treatments (many crops)
Captan 38% (4 lb/gal) flowable seed protectant (many crops)
Captan 25% seed protectant with molybdenum (soybeans)
Captan 20% - hexachlorobenzene 40% (wheat)
Captan 35% - Botran 35% (peanuts)
Captan 60% - Botran 20% seed protectant (peanuts

Captan 7.5% - Streptomycin 0.01% (potato seed pieces)
Captan 10% - pentachloronitrobenzene 20% (dust for infurrow or planter box use on cotton)

Fungicide - insecticide combinations, seed treatment:

Captan 60% - dieldrin 15% (many crops, slurry treatment)
Captan 12.5% - lindane 25% (many crops)
Captan 60% - lindane 15% (many crops)
Captan 65% - methoxychlor 5% (peas)
Captan 65% - methoxychlor 10% (many crops)
Captan 75% - methoxychlor 3% (many crops)
Captan 75% - methoxychlor 5% (many crops)
Captan 10% - diazinon 30% (some field crops)

Fungicides - soil treatment:

Captan 10% - pentachloronitrobenzene 10% soil fungicide (several crops)
Captan 30% - pentachloronitrobenzene 30% soil fungicide (several crops)

The sprayable and dust formulations for foliar application are registered for use on a wide variety of crops. The many different strengths and combinations of active ingredients are designed to meet a variety of growers' needs in different parts of the country. In the case of the seed protectant and soil treatment preparations, products designed for specific crops have been so identified in the above list.

According to information from several major captan formulators and marketers, the 50 and 80% wettable powder formulations and the 7.5 to 15% dust formulations are the most widely used formulations of captan.

Use Patterns of Captan in the United States

General - Captan is a broad spectrum contact fungicide effective against a fairly wide range of fungi causing plant diseases. It acts by inhibiting fungus mycelial growth. Captan does not cure or eradicate fungal infections on plants after they have become established and has to be applied prior to establishment of fungal infections.

Captan is registered and recommended for the control of foliage diseases on many fruit, vegetable, and ornamental crops; as a dip for the control of rots and damping off of cuttings, bulbs, and other planting stock; for the control of certain diseases on lawns and turf; for the control of rots of potato seed pieces, and as a protectant for the control of rots and damping off on many types of seeds.

In a project sponsored jointly by the Environmental Protection Agency and the Council on Environmental Quality (Midwest Research Institute-RvR Consultants, 1974[1]) the production, distribution, use, and environmental impact potential of 25 selected pesticides, including captan, were studied. In that study, it was determined that about 10.0 million pounds of captan AI were used for agricultural purposes in 1972. The manufacturers indicated that 1.0 million pounds were used for the home and garden sector. There were no significant uses of captan fy industrial, commercial or industrial organizations, or by governmental agencies.

Agricultural Uses of Captan - Surveys on the use of pesticides by farmers in the United States were conducted by the U.S. Department of Agriculture in 1964, 1966, and 1971 (Agricultural Economic Reports No. 131, published in 1968; No. 179, published in 1970; and No. 252, published in 1974). Table 22 summarizes the farm uses of captan from these surveys. It appears that the level of use of captan by farmers has remained relatively constant during the period covered by three USDA surveys. Estimates of the agricultural uses of captan in 1972 were developed by RvR Consultants used in the MRI-RvR study are also shown in Table 22. Although the 1972 usage appears to be greater, the USDA data is not directly comparable to the RvR estimates.

The USDA data is derived from interviews with farmers in selected counties throughout the United States. These interviews were conducted in nationwide programs whose principal purpose was the collection of data on farm production expenditures. The original, raw pesticide data were then expanded and adjusted by specific factors to translate them from the survey sample to the national universe. The USDA authors point out that the reliability of their data is related to the quantity of pesticides used, the number of acres treated, and the importance of the crop in the region. They state that the relative distribution of pesticides among crops and regions shown in their reports is more reliable than absolute quantities for individual crops and regions. Compared to all agricultural pesticides, captan is not one of the major products in regard to volume of use, and its use is scattered over many different crops, and over all regions of the country. Thus, there are many potential sources of error multiplication and/or extrapolation from too small a data base in a survey of this type.

The RvR estimates, on the other hand, were obtained by starting out with the estimated total domestic supply of captan. Based on information from trade sources, MRI estimates that captan stocks in inventory at the beginning of 1972 were very similar in size to those at the end of the year; the domestic supply of captan is assumed to be equal to domestic consumption. Manufacturer estimates indicate that about 1.0 million lb

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[1] Midwest Research Institute/RvR Consultants, "Production, Distribution, Use and Environmental Impact Potential of Selected Pesticides," (Draft), Council on Environmental Quality Control, Contract No. EQC-311 (March 1974).

Table 21. FARM USES OF CAPTAN IN THE U.S. IN 1964, 1966, 1971, AND 1972

Source	Year 1972 RvR[a]	 1971 USDA[b]	 1966 USDA[a]	 1964 USDA[b]
	Thousands of pounds of active ingredient			
Crops	9,600	6,013	6,587	5,661
Other farm uses	400	477	282	12
Total farm uses	10,000	6,490	6,869	5,673

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[a] RvR estimates. See text.

[b] USDA reports on "Quantities of Pesticides Used by Farmers," in 1964 (Agricultural Economic Report No. 131, published 1968); in 1966 (Agricultural Economic Report No. 179, published 1970); in 1971 (Agricultural Economic Report No. 252, in press).

of captan active ingredient were used in the home and garden sector in 1972. Since there were no significant uses of captan in the industrial/commercial sector or by Governmental agencies, MRI estimates that approximately 10-14 million pounds of active ingredient must have been used in agriculture.

In comparing this estimate to the USDA figures (Table 21), MRI does not believe that there was a 50% increase from 1971 to 1972 in the level of use of captan. MRI believes that the USDA surveys have tended to understate the actual quantities of captan used by farmers in the U.S.

Table 22 presents a further breakdown of the farm uses of captan in 1972 by regions and by major crops, based on RvR estimates developed in the MRI-RvR study. The following information sources were used in arriving at these estimates:

1. The three USDA surveys of pesticide uses by farmers mentioned above;
2. The annual USDA publication "Pesticide Review" (Agricultural Stabilization and Conservation Service);
3. Results of a survey of the Federal/State Cooperative Extension Services in all 50 states and in Puerto Rico conducted by RvR Consultants in 1973;
4. Analyses of state pesticide use recommendations;
5. Local and regional estimates on pesticide use volumes obtained from State Research and Extension personnel in personal communications;
6. Pesticide use reports from the states of Arizona, California, Illinois, Indiana, Michigan, Minnesota, and Wisconsin;
7. Data on pesticide uses supplied by the EPA Community Pesticide Studies Projects in Arizona, Hawaii, Idaho, Mississippi, South Carolina, Texas, and Utah;
8. Estimates and information obtained from basic producers of captan and other pesticides, and from pesticide trade sources;
9. Pesticide use surveys conducted recently by Wallaces' Farmer, Des Moines, Iowa; Prairie Farmer, Chicago, Illinois; and Wisconsin Agriculturist, Madison, Wisconsin; and
10. "Agricultural Statistics," an annual publication of the U.S. Department of Agriculture.

Data from all of these diverse sources was carefully analyzed, correlated, and cross-checked to arrive at the final estimates.

Table 22. ESTIMATED FARM USES OF CAPTAN IN THE U.S. BY REGIONS AND MAJOR CROPS (1972)

	Thousands of pounds of active ingredient				
Region	Apples	All other fruits and nuts	Vegetables	All other farm uses	Totals, All farm uses
Northeast[a]	2,200	1,050	150	100	3,500
Southeast[b]	1,100	800	Negligible	100	2,000
North Central[c]	1,400	400	100	100	2,000
South Central[d]	Negligible	350	50	100	500
Northwest[e]	1,000	500	100	100	1,700
Southwest[f]	Negligible	300	Negligible	Negligible	300
Total, all regions	5,700	3,400	400	500	10,000

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a/ Maine, New Hampshire, Vermount, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, Pensylvania.

b/ Maryland, Delaware, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida.

c/ Ohio, Indiana, Illinois, Michigan, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas.

d/ Kentucky, Tennessee, Arkansas, Louisiana, Mississippi, Alabama, Oklahoma, Texas.

e/ Montana, Idaho, Wyoming, Colorado, Utah, Washington, Oregon, Alaska.

f/ New Mexico, Nevada, Arizona, California, Hawaii.

Source: RvR estimates. See text.

Farm Uses of Captan by Regions - As previously mentioned, MRI estimates that about 10-14 million pounds of captan AI were used in agriculture in the U.S. in 1972 (Table 21). Of this total, the Northeastern states used about 3.5 million pounds, primarily on apples, other deciduous fruits, and small fruits. The Southeastern and North Central states used approximately 2 million pounds of captan each, followed by the Northwestern states (1.7 million pounds). The South Central (500,000 lb) and Southwestern (300,000 lb) states accounted for the balance.

Farm Uses of Captan by Crops - In analyzing the agricultural uses of captan by commodities (Table 22), it is obvious that this product is primarily a fruit fungicide. The use of captan on apples accounts for more than one-half of the total quantity used in agriculture in 1972. The largest use of captan on apples was in the Northeastern states (2.2 million pounds), followed by the North Central (1.4 million pounds), the Southeastern (1.1 million pounds), and the Northwestern (1 million pounds) states.

All other fruits and nuts (including citrus fruits, deciduous tree fruits other than apples, small fruits and berries, etc.) accounted for another 3.4 million pounds of captan consumption. The uses of captan on "all other fruits and nuts" were distributed regionally in much the same manner as the uses on apples. The largest quantity of captan in this category was used in the Northeastern states (1,050,000 lb), followed by the Southeastern states (800,000 lb). The remaining four regions each accounted for 500,000 lb or less.

Captan uses on all fruit and nut crops combined made up more than 90% of the total farm use of the product in 1972.

Uses of captan on vegetables, and for all other purposes combined totaled about 900,000 lb, distributed fairly evenly over all regions of the country. "All other uses" include foliar uses of captan on crops other than fruits and vegetables, uses for the protection of many types of seeds against rots and damping off; as a dip for control of rots and damping off of ornamental and horticultural planting stock; as a treatment for the control of rots on potato seed pieces, for the treatment of fruit and vegetable packing boxes against storage molds, etc.

Home and Garden Uses of Captan - Manufacturer estimates indicate that about 1.0 million pounds of captan AI were used by home gardeners in the U.S. in 1972. The use patterns of captan in this area were not investigated by MRI. No other published quantitative data is known to be available on nationwide home and garden pesticide uses.

In the home garden field, captan is widely used for the control of diseases on roses, other flowers, home-grown vegetables and fruits, and lawns. It is registered and recommended against blackspot on roses; powdery mildew, rust, leaf spot and other diseases on other flowers; against brown patch, leaf spot, damp-off, root rot and melting out on lawns; against blights and leaf spots on tomatoes and other vegetables; against scab, rots and leaf spots on apples, pears, stone fruits; and strawberries, and against similar fungal diseases on other homegrown ornamental and horticultural plants.

Nearly all retail outlets for home and garden pesticides throughout the entire U.S. carry one or more formulations containing captan.

Captan Uses in California - The State[1/] keeps detailed records of pesticide uses by crops and commodities which are published quarterly and summarized annually. Table 23 lists the uses of captan in California by major crops and other uses for the 4-year period (1970-1973).

In California, captan is not subject to the special restrictions and reporting requirements imposed upon the sale and use of pesticides designated as "injurious materials." For this reason, the California Department of Agriculture's statistics are probably less complete for captan than for restricted pesticides. However, the Department and others familiar with pesticide uses in California believe that these statistics include a substantial share of the captan actually used. Thus, while the data for individual and total uses may not be complete, they do provide a good indication for the use patterns of captan on California crops.

According to these state reports (Table 23), the total use volume of captan in California varied considerably, i.e., from a low of 115,000 lb in 1972 to a high of 292,000 lb in 1973. Similar variations occurred in the use of captan on individual crops.

Stone fruits (apricots, cherries, nectarines, peaches, plums, prunes) appear to account for the single biggest share of the total use of captan in California agriculture. Substantial quantities of the product are also used on grapes, almonds, walnuts, and strawberries. Uses on tomatoes, many other smaller crops, and some noncrop uses make up the balance.

[1/] California Department of Agriculture, Pesticide use reports for 1970, 1971, 1972 and 1973.

Table 23. CAPTAN USES IN CALIFORNIA BY MAJOR CROPS AND OTHER USES (1970-1973)

	Thousands of pounds of active ingredient			
	Year			
Crop	1973	1972	1971	1970
Stone fruits[a]	118	29	33	135
Almonds, walnuts	48	14	4	37
Strawberries	11	11	12	7
Grapes	52	28	24	8
Tomatoes	8	9	10	4
All other crop uses	39	17	59	14
Noncrop uses	16	7	1	5
Totals, all uses	292	115	143	210

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[a] Apricots, cherries, nectarines, peaches, plums, prunes, etc.

Source: California Department of Agriculture, op. cit. (1970 through 1973).

Tables 24 and 25 present the captan uses in California in detail, (by crops and other uses, number of applications, pounds of active ingredient, and number of acres treated) for 1972 and 1973, the two most recent years for which such data are available. In both years, captan was used in California on about 60 different crops.

The California Department of Agriculture's captan statistics cover primarily captan uses by farmers. They probably include very little of the captan used in the home and garden field.

At the present time, no other state records or publishes pesticide use data in comparable detail. Limitations of time and resources available for this task did not permit development of estimates on the uses of captan by states, crops, and other uses, beyond the detail provided in Tables 21 and 22.

Table 24. USE OF CAPTAN IN CALIFORNIA IN 1972, BY CROPS, APPLICATIONS, QUANTITIES, AND ACRES TREATED

Commodity	Applications	Lb	Acres*
Alfalfa	3	116.46	124.00
Almond	70	12,316.03	2,079.50
Apple	1	2.50	5.00
Apricot	12	2,149.20	538.00
U - Asparagus	2	195.00	1,350,000
P - Barley	2	388.82	361,700
P - Barley for seed	3	64.50	60,000
Beans, dry edible	3	528.00	176.00
P - Beans, dry edible	5	436.17	450,300
Beans, green or forage	1	192.50	55.00
P - Beans for seed	13	928.50	8,373,650
Berries	6	235.75	155.50
Boysenberry	3	261.00	87.00
Cabbage	6	55.00	52.00
Celery	39	1,234.79	685.50
Cherries, sweet	4	85.00	20.00
Citrus	11	16.39	144.20
City agency		12.00	
Collard	2	10.50	6.00
Cotton	6	1,793.17	1,156.00
County or city parks		2.27	
Cucumber or pickle	2	86.89	22.00
Grapefruit	6	391.53	95.40
Grape	112	27,790.12	8,917.00
Lettuce, head	56	1,480.65	1,027.90
Lettuce, leaf	21	321.50	229.25
Nectarine	31	1,940.44	471.50
Onion, dry	13	155.92	253.50
Orange	17	532.76	406.20
Ornamentals	2	1.00	0.50
Ornamental bedding plants	5	30.50	30.50
Other agencies		6,510.00	
Pasture, rangeland	1	3.12	73.00
Peach	145	18,588.49	3,550.60
Pear	3	312.50	75.00

Table 24. (Continued)

Commodity	Applications	Lb	Acres*
Pea	1	126.00	42.00
Pepper, bell	1	30.00	12.00
Plum	10	604.90	181.50
Potato	1	1.20	30.00
Prune	19	5,981.15	1,463.00
Raspberry	1	2.50	5.00
Residential control		1,074.74	
Rice	1	0.72	175.00
P - Rice	1	2,231.46	3,501,800
School district		66.87	
P - Sorghum for seed	7	1,353.21	877,200
Spinach	34	607.37	385.00
Squash, summer	1	15.00	5.00
State highway		38.00	
Strawberry	233	11,215.40	5,223.75
Structural control		3.36	
P - Sudangrass for seed	6	845.36	274,150
Tomato	75	9,523.64	2,818.00
University of California		0.05	
Vector control		0.76	
Walnut	7	2,144.02	409.00
P - Wheat for seed	1	22.48	25,800
Total	1,005	115,057.16	31,991.30

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* When the commodity listed is prefixed by P or U the amount listed in the respective acreage column is not acreage but one of the following, and is not tabulated in total acreage:

U = Miscellaneous Units P = Pounds

Source: California Department of Agriculture, op. cit. (1972).

Table 25. USE OF CAPTAN IN CALIFORNIA IN 1973, BY CROPS, APPLICATIONS, QUANTITIES, AND ACRES TREATED

Commodity	Applications	Lb	Acres*
Alfalfa	1	0.64	32.00
Almond	139	47,554.07	11,245.00
Apple	9	184.12	37.00
Apricot	125	22,874.32	5,273.00
P - Barley for seed	1	4.83	4,500
Beans, dry edible	1	0.24	12.00
Beans, green or forage	1	9.00	6.00
P - Beans for seed	14	1,220.12	1,063,194
Berries	1	90.00	30.00
Cabbage	3	2.08	101.00
Carrot	1	70.00	35.00
Cauliflower	1	1.04	111.00
Celery	22	580.00	337.50
Cherries, sweet	9	579.12	181.00
Citrus	5	2.06	104.00
City agency		1,684.28	
Corn, field	63	216.89	9,489.00
P - Corn, field	1	0.01	1,200
Corn for seed	5	103.43	1,075.00
P - Corn for seed	8	3.04	7,537
Cotton	6	1,141.64	891.00
Cottonseed	9	17.78	712.00
County agricultural commissioner		5.50	
County or city parks		6.42	
Cucumber or pickle	4	29.00	15.00
Flowers	92	592.13	206.37
Foliage	5	52.84	136.00
P - Grain	1	94.81	88,200
Grapefruit	8	510.25	88.50
Grape	411	52,005.38	20,533.30
Lemon	3	25.44	64.00
Lettuce, head	70	1,484.32	1,565.00
Lettuce, leaf	5	28.00	28.00
Melons	2	360.00	120.00
P - Miscellaneous	1	0.12	100

Table 25. (Continued)

Commodity	Applications	Lb	Acres*
Nectarine	26	937.00	298.00
Nonagricultural areas	1	0.40	1.00
Nursery stock	2	100.00	52.00
Onion, dry	59	1,494.02	852.25
P - Onion, dry	1	0.01	130
Orange	21	290.30	325.00
Ornamentals	16	579.50	304.50
Ornamental bedding plants	19	370.34	86.23
Other agencies		12,871.70	
Peach	225	28,648.10	6,938.25
Pear	5	316.50	101.00
Peas for seed	2	25,800.00	172.00
P - Peas for seed	1	12.65	36,000
Pepper, bell	1	0.52	100.00
Pimento	2	0.38	150.00
Plum	19	1,880.45	440.50
Prune	255	63,568.22	15,246.50
Residential control		1,121.38	
Rice	1	4.52	201.00
Safflower	2	1.81	140.00
School district		7.00	
Sorghum	7	12.09	675.00
Sorghum for seed	5	15.04	772.00
P - Sorghum for seed	3	391.60	228,030
Spinach	32	548.62	529.50
Squash, summer	5	217.00	96.00
State highway		37.50	
Strawberry	187	11,252.20	5,122.75
Structural control		6.20	

Table 25. (Continued)

Commodity	Applications	Lb	Acres*
P - Sudangrass for seed	2	1,596.60	1,143,650
Sugar beet	3	13.43	95.00
Tomato	92	8,019.07	4,196.75
University of California		2.05	
Vector control		0.12	
Walnut	2	318.04	83.00
P - Wheat	1	0.03	5,000
Total	2,024	291,967.31	89,406.50

---

* When the commodity listed is prefixed by P or U the amount listed in the respective acreage column is not acreage but one of the following, and is not tabulated in total acreage:

U = Miscellaneous Units P = Pounds

Source: California Department of Agriculture, *op. cit.* (1972).

PART III. MINIECONOMIC REVIEW

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This section contains a general assessment of the efficacy and cost effectiveness of captan. Data on the production of captan in the United States as well as an analysis of its use patterns at the regional level and by major crop, were conducted as part of the Scientific Review (Part II) of this report. For this reason, production and use data are reported in the Production and Use subsection (p. 122) of the Scientific Review.

Introduction

The efficacy and cost effectiveness of a specific pesticide should be measurable in terms of the increased yield or improved quality of a treated crop which in turn results in a greater income or lower cost than would be achieved if the pesticide had not been used. Thus, one should be able to pick an isolated test plot of a selected crop, treat it with a pesticide, and compare its yield with that of a nearby untreated test plot. The difference in yield should be the increase due to the use of the pesticide. The increased income (i.e., the yield multiplied by the selling price of the commodity) less the additional costs (i.e., the pesticide, its application and the harvesting of the increased yield) is the economic benefit due to the use of the pesticide.

Unfortunately, this method has many limitations. The data derived is incomplete and should be looked on with caution. Midwest Research Institute's review of the literature and EPA registration files revealed that experimental tests comparing crops treated with specific pesticides to the same crop without treatment are conducted by many of the state agricultural experimental stations. Only a few of these, however, have attempted to measure increased yield and most of this effort has been directed toward just a few crops such as cotton, potatoes, alfalfa and selected fruits. Most other tests on crops measure the amount of reduction in pest levels which cannot be directly related to yield.

Even the test plot yield data are marginally reliable, since these tests are conducted under actual field conditions that may never be duplicated again and may not be representative of general field use. Thus yield is affected by rainfall, fertilizer use, severe weather conditions, soil type, region of the country, pesticide infestation levels and the rate, frequency and method of pesticide application.

Because of these factors, yield tests at different locations and in different years will show a wide variance ranging from a yield decline to significant increases. For example, in a year of heavy pest infestation frequent pesticidal use can result in a high yield increase because the crop from the untreated test plot is practically destroyed. Conversely, in a year of light (or insignificant) infestation, the yield increase will be slight (or undetectable).

The use of market price to estimate the value received by the producer also has its limitations. If the use of the pesticide increases the yield of a crop and the national production is increased, then the market price should decline. According to J. C. Headley and J. N. Lewis (1967),[1/] a 1% increase in quantity marketed has at times resulted in a greater than 1% decrease in price. Thus the marginal revenue from the increased yield would be a better measure of value received.

A third limitation to the quantification of the economic costs and benefits is the limited availability of data on the quantities of the pesticide used by crop, disease or pest, the acres treated, and the number of applications. In most cases the amount of captan used on each crop or to treat each disease is not available.

As a result of these limitations an overall economic benefit by crop or pest cannot be determined. This report presents a range of the potential economic benefits derived from the use of captan to control a specific disease on a specific crop. This economic benefit or loss is measured in dollars per acre for the highest and lowest yield increase developed from experimental tests conducted by the pesticide producers and the state agricultural experimental stations. The high and low yield increases are multiplied by the price of the crop and reduced by the cost of the captan applied to generate the range of economic benefits in dollars per acre.

In certain industrial, institutional, commercial, consumer and governmental uses, economic benefits are difficult to assess by the above methods. Because of large uses for aesthetic reasons along with the absence of field test data no attempt was made to assign an economic benefit to this area.

[1/] Headley, J. C., and J. N. Lewis, The Pesticide Problem: An Economic Approach to Public Policy, Resources for the Future, Inc., Washington, D.C. (1967).

Captan was first introduced as a fungicide in 1948 and has found its largest use for treating fruits and vegetables to prevent scab and rot. Not only does it control diseases without burning foliage and fruit, it promotes greater carbohydrate production and storage by plant tissues, resulting in heavier foliage growth, increased fruit set and better fruit color and finish. Captan is available as a variety of wettable powder and dust formulations.

Data on the efficacy and economic benefits due to the use of captan have been reported for selected fruits and vegetables. These include benefits from the control of scab and rot on apples, brown rot and scabs on peaches, gray mold on strawberries, potato scab on potatoes, and seed diseases of soybeans. These results are summarized in the following paragraphs.

Apples

Efficacy Against Pest Infestation - Approximately 5,700,000 lb of captan were used in 1972 for fungicidal control of apple trees. Captan is a good all-round fungicide for control of scab and rots; it provides good finish and is often applied as a combination with other fungicides and insecticides.

A review of available literature and the EPA registration files has revealed numerous experiments which determined yields of apples treated with captan. Unfortunately, most of these experiments compare captan-treated apple trees with other chemicals. Most of these experiments were conducted in the 1950 to 1954 period and often relate the yield changes in bushels per tree. Others report the use of captan in terms of pounds per hundred gallons of water but do not relate it to the quantity applied to the tree.

A review of Fungicide and Nematocide Tests published by the American Phytopathological Society revealed numerous tests conducted on apple trees but most reported the results in terms of percent control of fruit scab or percent fruit infection which is difficult to relate to yield. However, many indicated that they used 3 to 5 gal. of spray per tree. Since a 50% wettable powder formulation (50W) is recommended for apples in a mixture containing 2 lb of this formulation per 100 gal of water this would result in a use of 0.06 to 0.10 lb/tree or an average of 0.08 lb of the formulation per tree (0.04 lb active ingredient (AI) per tree).

Yields from tests varied from a low of 3.0 bushels per tree from a summary of tests in Pennsylvania in 1952 to a high of 30.1 bushels per tree from tests conducted on Baldwin apples in Medina, New York, in 1954.

Since there were no tests which compared captan - treated trees with untreated trees actual yield benefits are impossible to determine. Test results, however, have shown the untreated trees most often will have up to 100% scab or rot which would render the fruit worthless or significantly reduce its value.

The yield of apples following application of captan and other fungicides is illustrated in the following table:

Table 26. YIELD (BUSHELS/TREE) FROM CAPTAN (ORTHOCIDE 50W) SPRAYED APPLE TREES

Test 1 - University of Maryland, Dr. Castillo Graham -

	Apple Variety and Year						
	Golden Delicious		Stayman		York		
Treatment	1951	1953	1951	1953	1952	1953	1954
Captan	7.0	7.0	12.0	13.7	15.0	9.5	4.7
Standard Fungicides*	4.0	4.0	4.0	5.2	8.0	5.0	2.3

Test 2 - California Spray Chemical Company, Medina, N.Y. -

	Baldwin variety in year	
Treatment	1953	1954
Captan	20.0	30.1
Standard Fungicide**	15.0	23.6

Test 3 - University of Maine, Dr. M. T. Hilborn -

	McIntosh variety in year		
Treatment	1952	1953	1954
Captan	17.66	18.72	26.51
Standard Fungicide**	14.80	16.74	15.32

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* A combination of two commercial standard fungicides.

** A commercial standard fungicide.

Table 26. (Continued)

Test 4 - R. D. Wessel, Medina, N.Y. -

Treatment	Baldwin variety in year	
	1953	1954
Captan	19.9	26.6
Standard Fungicide**	21.7	19.7

Test 5 - Rutgers University, Dr. R. H. Davies -

Treatment	Variety	
	Red Delicious	Stayman
Captan	7.1	11.1
Standard Fungicide**	4.3	4.5
Standard Fungicide**A+ Captan	6.7	9.2
Standard Fungicides*	5.3	6.3
Standard Fungicide**B+ Captan	6.6	5.9

Source: California Spray Chemical Company and Stauffer Chemical Company, EPA Pesticide Petition No. 124 (undated).

Table 27. YIELD AND PROFITS FROM USING ORTHOCIDE 50W IN SELECTED STATES

State	Year	Yield (bushels/tree)	
		Orthocide 50W	Sulfur - Ferbam
Pennsylvania	1953	22.0	1.7
Maryland	1951	12.0	8.0
Maryland	1951	7.0	3.0
Maryland	1952	15.0	7.0
West Virginia	1952	14.5	3.5
Pennsylvania	1953	10.5	1.7
Pennsylvania	1952	4.6	2.3
Pennsylvania	1953	4.0	1.1
Maryland	1952-53	4.7	2.4
Maryland	1953	9.5	4.5
New York	1953	20.0	5.0
New Jersey	1953	4.0	2.75
Rhode Island	1952	4.7	2.1
Pennsylvania	1952	3.0	1.3
Average		9.0	3.1

Source: California Spray Chemical Company and Stauffer Chemical Company, EPA Pesticide Petition No. 124 (undated).

Cost Effectiveness of Pest Control - If the extreme of complete destruction of the apple crop without the use of captan is assumed, then a range of benefits can be determined. The average price received for apples in 1972 was $0.64/lb and there is an average of 40 lb of apples in a bushel (Agricultural Statistics 1973).[1] Prices for captan 50W range from $0.75 to $0.90/lb (McGlohon, 1974).[2] This would average $0.825/lb, equivalent to $1.65/lb of active ingredient. At a use of 0.4 lb AI/tree, the captan would cost $0.66/tree.

With apples at $0.064/lb, a 40-lb bushel of apples would yield an income of $2.56. At this price the additional income for the yield range of 3.0 to 30.1 bushels per tree would vary from $7.68 to $77.06/tree. Subtracting the captan cost of $0.66 would yield an economic benefit range of $7.02 to $76.40/tree from the use of captan.

Peaches

Efficacy Against Pesticide Infestation - Captan is used on peach trees to control brown rot. A review of available literature revealed one test which related yields to captan use. W. J. French (1969)[3] conducted tests at the University of Florida in 1968 to evaluate captan 50W against brown rot and scab on peaches. Seven treatments of captan 50W were applied to the trees. The captan was used at a rate of 3 gal/tree and was formulated with water at 2 lb/100 gal. (1 lb AI per 100 gal.)

At these rates the captan use would amount to 0.03 lb AI per tree for each spray and 0.21 lb AI per tree for the season. A yield of 146 lb/tree was obtained for the treated trees whereas an untreated plot yielded 104 lb of peaches. This resulted in an increase of 42 lb of fruit from the use of captan.

Cost Effectiveness of Pest Control - The price of peaches in 1972 averaged $0.07/lb (Agricultural Statistics 1973). At a yield increase of 42 lb/tree this would produce an additional revenue of $2.94/tree. At a price of captan of $1.65/lb of active ingredient (McGlohon, 1974) and a use of 0.21 lb/tree captan costs per tree would be $0.35. Subtracting the captan costs from the additional revenue would yield an economic benefit of $2.59/tree for the use of captan to prevent brown rot and scab.

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[1] United States Department of Agriculture, Agricultural Statistics 1973.

[2] McGlohon, Norman E., Head Extension Plant Pathology Department, University of Georgia, College of Agriculture, Athens, Georgia, personal correspondence with David F. Hahlen (July 10, 1974).

[3] French, W. J., Abstr. 78, "Peach," Fungicide and Nematocide Test Results of 1969, the American Phytopathological Society (1969).

Strawberries

Efficacy Against Pest Infestation - Captan is used to prevent gray mold on strawberries. Normally it is applied at a rate of 4 to 6 lb/acre for the 50% wettable powder, and 40 lb/acre for the 7.5% dust.

A review of available literature and EPA registration files has produced experiments which relate yields to captan use. All of the EPA data consisted of experiments conducted from 1952 to 1954. Recent data is presented in the following tables:

Table 28. RESULTS OF CAPTAN APPLICATION ON STRAWBERRIES

	Application rate			Yield	Increase		
Captan	lb/acre	No.	lb AI/acre	(qt/acre)	qt/acre	lb/acre	Source
7.5% Dust	50	5	18.75	3,119	1,582	2,370	a/
50% Powder	6	5	15.0	3,261	1,724	2,586	a/
7.5% Dust	50	5	18.75	7,152	2,797	4,196	a/
50% Powder	6	5	15.0	5,487	1,132	1,698	a/
7.5% Dust	50	5	18.75	4,732	2,205	3,308	a/
50% Powder	6	5	15.0	5,216	2,689	4,033	a/
7.5% Dust	50	5	18.75	4,992	1,776	2,664	a/
50% Powder	6	5	15.0	5,592	2,376	3,564	a/
50% Powder	6	3	9.0	15,400	5,800	8,700	b/

a/ California Spray Chemical Company and Stauffer Chemical Company, "Captan," Petition No. 124 (undated).
b/ Baldwin, R. E., "Strawberries," Fungicide and Nematocide Test Results of 1968, the American Phytopathological Society (1968).

The results of these tests show that increases in yield of strawberries ranged from a low of 1,698 lb/acre with an application of 15.0 lb AI/acre of captan, to a high of 8,700 lb/acre with an application of 9.0 lb AI/acre of captan.

The yield of strawberries following application of Orthocide (captan) is illustrated in the following tests[1]:

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[1] California Spray Chemical Company and Stauffer Chemical Co., EPA Pesticide Petition No. 124.

Table 29. YIELD RESULTS (QUARTS/ACRE) AND PROFITS FOR FIVE APPLICATIONS OF CAPTAN TO STRAWBERRY PLANTS

Test 1 - Gray mold control test, Haddenfield, New Jersey, 1953 -

Treatment	Rate Lb/Acre	Qt/Acre	Gross receipts at $.35/Qt
Captan 7.5 Dust	50	3,119	$1,091.65
Captan 50W	6	3,261	1,141.35
Standard Fungicides*	-	2,186	765.10
Check		1,537	537.95

Test 2 - Gray mold control test, Haddenfield, New Jersey, 1954 -

Treatment	Rate Lb/Acre	Qt/Acre	Gross receipts at $.35/Qt
Captan 7.5 Dust	50	7,152	$2,503.20
Captan 50W	6	5,487	1,920.65
Check		4,355	1,524.25

Test 3 - Gray mold control test, Moorestown, New Jersey -

Treatment	Rate Lb/Acre	Qt/Acre	Gross receipts at $.35/Qt
Captan 7.5 Dust	50	4,732	$1,656.20
Captan 50W	6	5,216	1,825.60
Check		2,527	884.45

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* A combination of two commercial standard fungicides.

Cost Effectiveness of Pest Control - At a price of $1.65/lb AI for captan 50W (McGlohon, 1974), the respective costs would be $24.75 and $14.85/acre.

The average price of strawberries in 1972 was $24.00/cwt (Agricultural Statistics 1973). At this price, yields would generate an additional income ranging from $407.52/acre to $2,088.00/acre. Subtracting the captan cost would result in economic benefits ranging from $328.77 to $2,073.15/acre due to the use of captan to control gray mold.

Uses on Vegetables

Although 400,000 lb of captan were used in 1972 to treat vegetable crops its use is probably declining due to the development of improved fungicides. Recent literature indicates that captan is not being evaluated during fungicidal tests conducted by the various agricultural field stations. McGlohon (1974) states that although captan has a label registration for vegetables in Georgia, there are other fungicides that are more effective.

Potatoes -

Efficacy Against Pest Infestation - Captan has been used as a fungicide for treatment of potato seeds. Cetas (1966)[1/] has conducted yearly tests at the Cornell University, Long Island Research Farm, to evaluate captan and other fungicides for the control of potato scab (*Rhizoctonia solani*). The results of these tests are shown in Table 30.

Table 30. RESULTS OF CAPTAN APPLICATION TO POTATO SEED PIECES

Captan Content of Formulation (%)	Rate lb/cwt seed	Rate lb AI/ acre	Yield (cwt/acre)	Gain (cwt/acre)	Source
7.5	1	1.3	351	44	a/
7.5	1	1.3	247	33	b/
7.5	1	1.3	283	36	c/
7.5	1	1.3	277	30	c/
15.0	1	2.6	303	56	c/
7.5	1	1.3	383	35	d/
15.0	1	2.6	406	58	d/
7.5	1	1.3	301	15	d/
15.0	1	2.6	315	31	d/

a/ Cetas (1966)[1/]

b/ Cetas, Robert C., "Potato," Fungicide and Nematocide Test Results of 1967, American Phytopathological Society, St. Paul, Minn., pp. 120-121 (1967).

c/ Cetas, Robert C., "Potato," Fungicide and Nematocide Test Results of 1968, American Phytopathological Society, St. Paul, Minn., p. 111 (1968).

d/ Cetas, Robert C., "Potato," Fungicide and Nematocide Test Results of 1969, American Phytopathological Society, St. Paul, Minn. (1969).

[1/] Cetas, Robert C., "Potato," Fungicide and Nematocide Test Results of 1966, American Phytopathological Society, St. Paul, Minn. pp. 72-73 (1966).

The results of these tests show that yield increases range from 15 to 58 cwt/acre.

Cost Effectiveness of Pest Control - The price of potatoes averaged $2.55/cwt in 1972 (Agricultural Statistics, 1973). At this price the additional income at the above yields would vary from $38.25 to $147.90 per acre.

A 7.5% dust formulation of captan was used at a rate of 1.0 lb/cwt of seed potatoes. Approximately 17.2 cwt of seed potatoes are required per acre of potatoes (Agricultural Statistics, 1973.) This would require 17.2 lb/acre of the formulation (1.3 lb AI/acre).

The price of captan (7.5%) is about 15c/lb ($2.00/lb AI) (California Spray-Chemical, 1974[1]). Subtracting the captan cost from the additional income at the respective application rates would result in economic benefits ranging from $35.65 to $142.50 per acre for the use of captan on potatoes.

Soybeans -

One test was reported in the 1967 issue of Fungicide and Nematocide Test Results concerning the use of captan on soybean seedlings. A. Y. Chambers (1967)[2] of the Tennessee Agricultural Experimental Station found taht soybean yield increased from 33.3 bushels/acre to 37.0 bushels/acre when the seed was treated with 3 oz of 50% captan per 100 lb of seed. He reported that 30 lb of seed were required per acre. At this rate captan (AI) use per acre would amount to 0.028 lb. This increase would amount to a yield increase of 3.7 bushels/acre. At a 1972 average price of $3.49/bushel for soybeans (Agricultural Statistics, 1973) the additional income would be $12.91/acre. At captan prices of $1.65/lb (AI) (McGlohon, 1974) the cost of 0.028 lb would be $0.05/acre when captan is used as a fungicide.

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[1] California Spray-Chemical Corporation, Kansas City, Missouri, Personal communication to Mr. David F. Hahlen (Midwest Research Institute, Kansas City, Mo.) (July 15, 1974).

[2] Chambers, A. Y., "Soybeans," Fungicide and Nematocide Test Results of 1968, American Phytopathological Society, St. Paul, Minn., p. 124 (1967).

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